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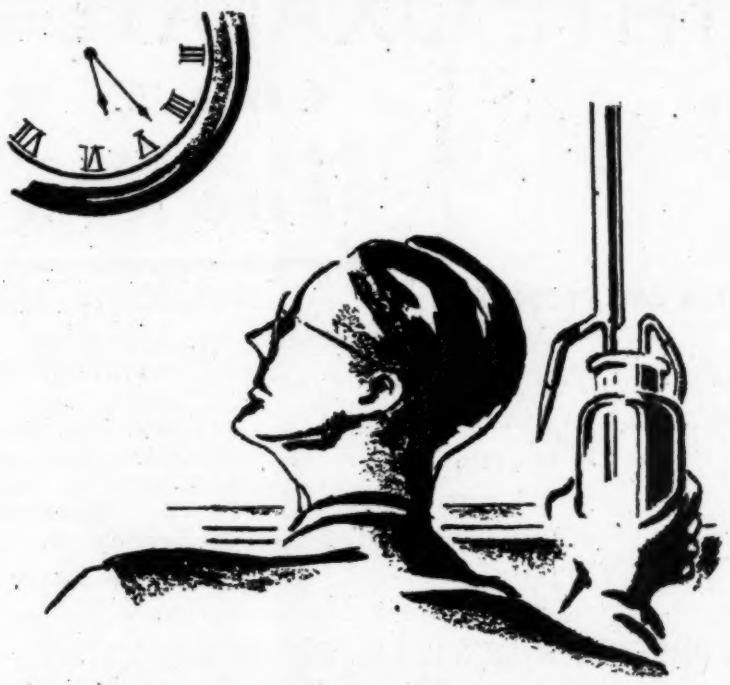

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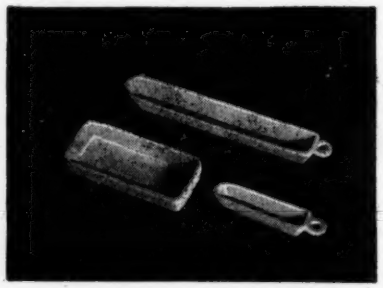

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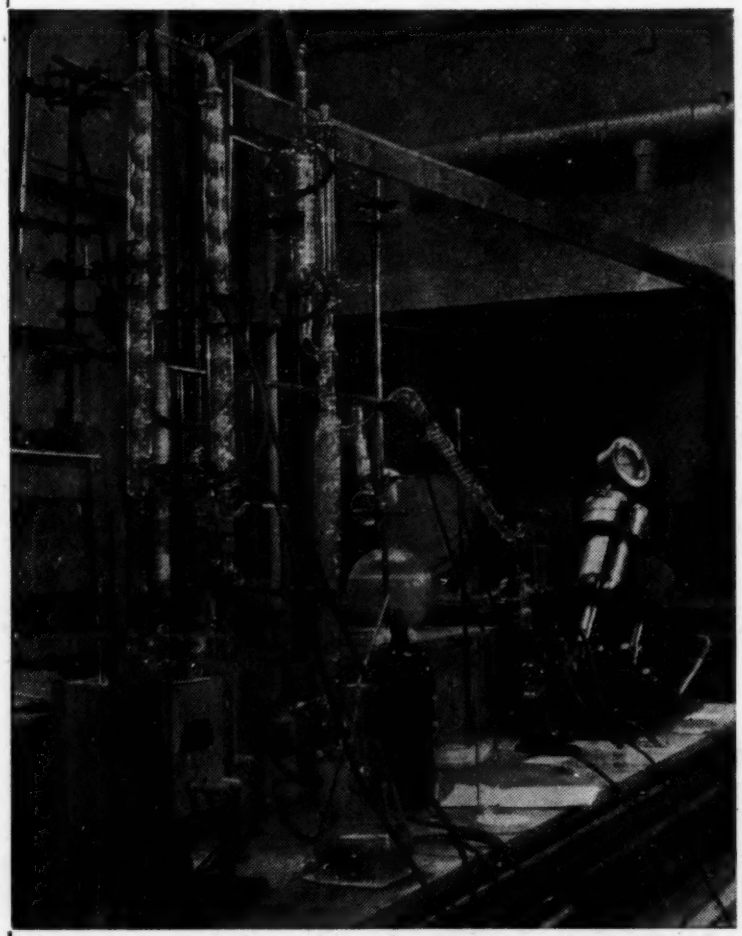

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33. *Experiments on the Interaction of Hydroxy-compounds and Phosphorus and Thionyl Halides in the Absence and in the Presence of Tertiary Bases. Part I. Optically Active β-Octanol, Ethyl Mandelate, and Phenylmethylcarbinol.*

By William Gerrard.

During addition of phosphorus trichloride to (+)-β-octanol and to ethyl (−)mandelate, the chloride RCl and the hydrogen phosphite $P(OR)_2 \cdot OH$ were produced; but reversed order of mixing resulted in formation of the *chlorophosphite* $PCl_2 \cdot OR$, which did not decompose into the chloride RCl. (+)-α-Chloroethylbenzene was formed from (−)phenylmethylcarbinol during the actual mixing at 0° in either order, no evidence of formation of the chlorophosphite being discernible. (+)*Tri-β-octyl phosphite* and phosphorus trichloride formed at 15° an equilibrium mixture of the two chlorophosphites, $PCl_2 \cdot OR$ and $PCl(OR)_2$, and the trichloride.

Mixing at 0°, in either order, of thionyl chloride with (+)-β-octanol and with ethyl (−)mandelate resulted in formation of an equilibrium mixture of the chlorosulphinate, $OR \cdot SOCl$, the sulphite, R_2SO_3, and thionyl chloride, but a little chloride RCl was formed at this stage. (−)-α-Chloroethylbenzene, however, was formed from (−)carbinol during the actual mixing at 0°.

Whereas ethyl (−)mandelate, (+)-β-octanol, and (−)phenylmethylcarbinol formed the corresponding phosphites when mixed with pyridine in ethereal solution and treated with phosphorus trichloride, and the mandelate and β-octanol formed the corresponding sulphites under equivalent conditions, yet (−)phenylmethylcarbinol formed (+)-α-chloroethylbenzene during the actual addition of thionyl chloride, there being no sign of formation of sulphite. On the other hand, ethyl chlorosulphinate used in place of thionyl chloride gave the mixed sulphite, (−)-*α-phenylethyl ethyl sulphite*, which with thionyl chloride gave the non-inverted α-chloroethylbenzene. An equilibrium mixture of chlorosulphinate and unchanged thionyl chloride and sulphite was formed by the action of thionyl chloride and (+)di-β-octyl sulphite. Explanations in terms of mechanisms which depend on oriented collisions on the "front" or on the "back" of the asymmetric carbon atom cannot be disregarded.

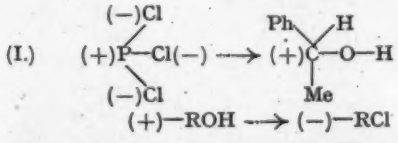
Probable modes of interaction of the compounds stated in the title have been discussed by the author (J., 1936, 688; 1939, 99; 1940, 218, 1464) where full references to literature were given. It is intended to examine in more detail the history of each relevant system from the time when the reagents are mixed to the stage where the C–O bond is broken and the chlorine atom becomes attached; and at the same time to establish a rational connection between the quantities and mode of mixing of the reagents on the one hand, and the nature and yields of products on the other. In this project, the experimental results of Kenyon and Phillips and of McKenzie and their co-workers are of value, but these reactions require detailed attention such as that given (*e.g.*, by Cowdrey, Hughes, Ingold, Masterman, and Scott, J., 1937, 1252) to the counter-process of hydrolysis of the chlorides (RCl).

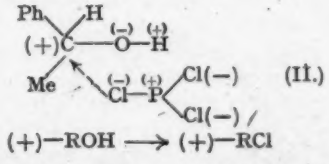
Reactions with Phosphorus Trichloride.—The main effect of adding (+)-β-octanol (Table, A) and ethyl (−)mandelate (Table, B) severally to phosphorus trichloride (>1 mol.) at 0° was the production of chlorophosphites, $PCl_2 \cdot OR$ and $PCl(OR)_2$, and not chloride, RCl. (−)-β-*Octyloxyphosphorus dichloride* and (+)*di-β-octyloxyphosphorus chloride* were distilled without decomposition. The dichloride (b. p. 119°/15 mm.) remained unchanged on standing for 14 days; it decomposed to octylene at 150°/754 mm., but was essentially unaffected by heating with pyridine or its hydrochloride. (−)-α-*Carbethoxybenzyloxyphosphorus dichloride* (b. p. 105—108°/2 mm.) was obtained by distilling the primary mixture obtained from the trichloride and (−)mandelate. It did not yield the chloroacetate on being heated for 30 minutes with pyridine or its hydrochloride.

Continuation of addition of (+)-β-octanol beyond 1 mol. did yield a little (−)-β-octyl chloride, but this was probably formed by the mechanism $PCl(OR)_2 + ROH \longrightarrow P(OR)_3 + HCl \longrightarrow P(OR)_2 \cdot OH + RCl$.

During the addition, at 0°, of the trichloride to (+)-β-octanol and to (−)mandelate, the following reaction appeared to take place: $PCl_3 + 3ROH \longrightarrow P(OR)_3 + 3HCl \longrightarrow P(OR)_2 \cdot OH + RCl$, support for this view being afforded by the readiness with which (+)*tri-β-octyl phosphite* reacted with hydrogen chloride at 0° and afforded (−)-β-octyl chloride and (+)di-β-octyl hydrogen phosphite.

By either order of addition, (−)phenylmethylcarbinol formed (+)-α-chloroethylbenzene during the mixing with the trichloride at 0° (Table, C), and it is possible that the mechanism is one of oriented collision, *e.g.*, mechanisms (I) and (II). In mechanism (II), the (−)Cl becomes attached to the (+)C before the





(+)P can claim the (−)O. With the other two hydroxy-compounds the (+)P becomes attached first, and so forms the stable chlorophosphite. When the trichloride was added to the hydroxy-compound, hydrogen chloride played a significant part; even when the operation was conducted in ethereal solution in the presence of solid potassium carbonate, as was done by Kenyon, Phillips, and Taylor in the case of phenylmethylcarbinol (see Experimental), the hydrogen chloride may not have been removed quickly enough.

The primary product from the addition of the trichloride to (+)-β-octanol and pyridine in ethereal solution appeared to be a good specimen of (+)tri-β-octyl phosphite; distillation, however, afforded both this and

No.	Order of mixing.†	Reagent, mols.	Main products.	Yield, %.	α_D.	Notes.
			(A) *Reactions of* (+)-β-*octanol*, α_D + 8·0° (1 *mol.*).			
1	⟶	PCl_3, >1	RCl	none	—	—
			PCl_2OR	80	− 34·5°	—
			$PCl(OR)_2$	12	+ 0·7	—
2	⟵	,, ½	RCl	27	− 30·4	(1)
			$P(OR)_2$·OH	58	+ 15·8	
3 *	⟵	,, ½	RCl	none	—	
			$P(OR)_2$·OH	33	+ 14·5	(2)
			$P(OR)_3$	50	+ 0·8	
4	⟶	$SOCl_2$, 2	RCl	none	—	—
			RO·SOCl	50	—	—
			$SO(OR)_2$	34	− 16·8	(3)
5	⟶	,, 1	RCl	7	—	—
			RO·SOCl	28	—	—
			$SO(OR)_2$	40	− 16·2	—
6	⟵	,, 1	RCl	trace	—	—
			RO·SOCl	29	—	—
			$SO(OR)_2$	43	− 16·5	—
7 *	⟵	,, ½	$SO(OR)_2$	84	− 17·5	—
			(B) *Reactions of ethyl mandelate* (1 *mol.*), α_D −131° *for expts.* 1 *and* 2, +120° *for* 3, 4, *and* 5.			
1	⟶	PCl_3, >1	RCl	none	—	—
			PCl_2OR	28	−117·5	—
			Undist. res.	—	—	(4)
2	⟵	,, ½	RCl (Cl, 12·6%)	26	+ 40·5	(1)
			$P(OR)_2$·OH	50	− 93·6	
3	⟶	$SOCl_2$, 1·1	RCl	15	+ 97·7	(5)
			RO·SOCl	80	—	—
			RCl	90	+ 84·2	(6)
4	⟵	,, ½	RCl (Cl, 13·6%)	52	+ 92·6	(1)
			$SO(OR)_2$	24	—	—
5 *	⟵	,, ½	$SO(OR)_2$	88	+124·2	—
			(C) *Reactions of phenylmethylcarbinol* (1 *mol.*), α_D −40·3° *for expts.* 1—4, −41·3° *for* 5, +20·5° *for* 6 *and* 7.			
1	⟶	PCl_3, >1	RCl ‡	75	+ 20·2	(1)
2	⟶	,, 1	RCl ‡	63	+ 19·9	(1)
			$P(OR)(OH)_2$	10·8	—	—
3	⟵	,, ⅓, ⅔, or 1	RCl ‡	60	+ 19·9	(1)
4 *	⟵	,, ⅔	Phosphite (6·7 g. from 7·3 g. ROH)	—	− 65·2	(1)
5	⟶	$SOCl_2$, 1	RCl ‡	80	− 50·9	(1)
6	⟵	,, 1	RCl ‡	66	+ 14·6	(1)
7 *	⟵	,, ⅔	RCl ‡	50	− 22·4	(1)
			Residue (3·5 g. from 12·2 g. ROH)	—	+ 69·6	(1)

* Denotes addition of 1 mol. of pyridine.
† ⟶ Denotes that octanol was added *to* the reagent, and ⟵ *vice versa*.
‡ Formed during mixing.

Notes: (1) After aqueous treatment. (2) After distillation. (3) Estimated by cold aqueous treatment. (4) 4·4 G. from 8·2 g. of mandelate. (5) Primary product. (6) After 4 days, then aqueous treatment.

(+)di-β-octyl hydrogen phosphite, and it has not been ascertained whether the di-ester was present before the distillation. Ethyl (−)mandelate and (−)phenylmethylcarbinol yielded primary products which appeared to have a similar nature to that from β-octanol, but they could not be distilled. An equilibrium mixture of chlorophosphites, tri-β-octyl phosphite, and phosphorus trichloride was formed when the last two were mixed. The phosphite product from (−)phenylmethylcarbinol, however, rapidly yielded (+)-α-chloroethylbenzene when treated with the trichloride.

Reactions with Thionyl Chloride.—By either order of addition at 0°, this reagent produced with (+)-β-octanol an equilibrium mixture of thionyl chloride, (−)di-β-octyl sulphite, and (−)-β-octyl chlorosulphinate, excess of thionyl chloride favouring the last compound. The conclusion that the formation of sulphite is rapid compared with the rate of interaction of thionyl chloride and sulphite is supported by determining the amount of sulphite immediately after mixing, and by observation of the slow rise in rotatory power of a mixture of thionyl chloride and (−)di-β-octyl sulphite (Procedure 10). Heating such a mixture with pyridine hydrochloride [a system similar to that which results when thionyl chloride (1 mol.) is added in the cold to a hydroxy-compound (1 mol.) and pyridine (1 mol.)], probably has two main effects: (1) the rise in temperature increases rate of interaction of the sulphite and thionyl chloride; (2) the hydrochloride facilitates decomposition of the chlorosulphinate by an undetermined mechanism. Preliminary experiments with pyridine hydrobromide and a chlorosulphinate failed to show that the former is a source of bromide ions which might become attached to the asymmetric carbon atom.

The primary product obtained by adding ethyl (+)mandelate (α_D + 120·1°) to thionyl chloride (Procedure 7) was treated in four different ways: (1) Aqueous treatment yielded ethyl (+)mandelate mixed with a little chloroacetate (Cl, 2·7%), and since hydrogen chloride was evolved in quantity during the mixing, the mandelate

must have resulted from the hydrolysis of the chlorosulphinate. (2) During 4 days, the rotatory power and the readily hydrolysed Cl and SO_2 content fell, and aqueous treatment then yielded the (+)chloroacetate, $\alpha_D^{18°}$ +84·2° (Cl, 17·1%). (3) Warming with pyridine hydrochloride followed by aqueous treatment gave the (−)chloroacetate in excellent yield ($\alpha_D^{20°}$ −4·6°) (Cl, 17·8%). (4) Standing for 12 hours with pyridine in ethereal solution followed by aqueous treatment yielded a mixture of mandelate and chloroacetate ($\alpha_D^{22°}$ −20·1°) (Cl, 14·1%), and (+)*bis-α-carbethoxybenzyl sulphite* ($\alpha_D^{22°}$ +108°).

Both (+)-β-octanol and ethyl (−)mandelate gave excellent yields of the corresponding sulphites through the agency of thionyl chloride and pyridine.

(−)Phenylmethylcarbinol yielded, during the mixing with thionyl chloride at 0°, (−)-α-chloroethylbenzene, the (+)isomer being formed if pyridine was also present. Furthermore, (−)-α-chloroethylbenzene was obtained by the action of thionyl chloride on (−)-*α-phenylethyl ethyl sulphite*, prepared from ethyl chlorosulphinate and (−)phenylmethylcarbinol through the agency of pyridine.

Mechanisms similar to (I) and (II), not involving the actual formation of the chlorosulphinate of phenylmethylcarbinol, cannot be disregarded. It is possible that pyridine may form the hydrogen bond, (+)C–O–H:NC_5H_5, and slightly reduce the speed of approach of the thionyl chloride molecule, thus giving some advantage to the "inversion" attack at the back of the molecule. Alternatively, the NC_5H_5 may direct the "non-inversion" attack to itself and again give the inversion attack some advantage.

Experimental.

Rotatory powers were determined in a 50-mm. micro-tube, but are recorded for l = 10 cm. Where aqueous treatment was used it is specified, and all ethereal solutions were dried before evaporation. A solution of sodium carbonate was especially used in extracting the respective dihydrogen phosphite, which was then recovered from the carbonate solution by acidification and extraction with ether.

Procedure (1). *Addition of Hydroxy-compound to Phosphorus Trichloride.*—The hydroxy-compound was added dropwise from a tap funnel fitted to a distillation flask containing the trichloride agitated by a stream of carbon dioxide or hydrogen and kept at 0°. The side tube of the flask was attached to an apparatus for absorbing the hydrogen chloride evolved. When addition was complete, the product was allowed to warm to room temperature, and then treated as specified.

(+)-β-Octanol (Kenyon, J., 1922, **121**, 2540) ($\alpha_D^{18°}$ +8·0°, 6·5 g., 1 mol.) and the trichloride (13·7 g., 2 mols.) gave, after being at 100°/15 mm. for 2 hours, (−)-*β-octyloxyphosphorus dichloride* (9·2 g.), b. p. 83—84°/2 mm., b. p. 118—119°/17 mm., $\alpha_D^{18°}$ −34·5°, $d_4^{18°}$ 1·0749, $d_4^{25°}$ 1·0683, $d_4^{35°}$ 1·0588, $n_D^{19°}$ 1·4669 (Found: Cl, 30·7; P, 13·5. $C_8H_{17}OCl_2P$ requires Cl, 30·7; P, 13·4%), (+)*di-β-octyloxyphosphorus chloride* (1·0 g.), b. p. 135—140°/2 mm., $\alpha_D^{18°}$ +0·7, $n_D^{20°}$ 1·4430 (Found: Cl, 10·5; P, 9·9. $C_{16}H_{34}O_3ClP$ requires Cl, 10·9; P, 9·6%), and an orange-coloured residue (0·8 g.), but no β-octyl chloride. The dichloride is a colourless liquid which fumes in moist air and is vigorously hydrolysed by water; 4·6 g. were poured on ice, and the ethereal extract, after being washed with a solution of sodium carbonate, gave only 0·2 g. of residue. From the carbonate solution, (+)-*β-octyl dihydrogen phosphite* (2·7 g.), $\alpha_D^{16°}$ +7·0°, $d_4^{18°}$ 1·0210, $d_4^{50°}$ 0·9914, $n_D^{18°}$ 1·4400 (Found: P, 15·9. $C_8H_{19}O_3P$ requires P, 16·0%), was obtained; Houssa and Phillips (J., 1932, 108) found evidence of formation of this phosphite in their experiment with pyridine as a reagent.

After standing at room temperature for 14 days, the dichloride had $d_4^{25°}$ 1·0711, $n_D^{18°}$ 1·4651, $\alpha_D^{18°}$ −31·6°, and 96% of it distilled as dichloride, with original physical properties, and left a residue. No β-octyl chloride was obtained. The dichloride (4·8 g.), when heated at atmospheric pressure, decomposed steadily at 150°. An orange-coloured solid (0·12 g.) was deposited, hydrogen chloride (0·56 g.) evolved, and a colourless distillate (2·3 g.) obtained. The aqueous washing of the last contained hydrochloric acid (0·78 g.) and some phosphite ion, and therefore most of the chlorine in the system was accounted for. The washed distillate was octylene (1·4 g.), b. p. 123°/756 mm. (+)-β-Octanol (6·5 g., 1 mol.) and the trichloride (3·5 g., 0·5 mol.) gave (i) (−)-β-octyl chloride (1·3 g.), b. p. 63°/16 mm., $\alpha_D^{18°}$ −30·2°, $n_D^{18°}$ 1·4273; (ii) (−)-β-octyloxyphosphorus dichloride (2·9 g.), b. p. 75°/1 mm., $\alpha_D^{18°}$ −34·1° (Found: Cl, 30·6%); (iii) a mixture of di-β-octyloxyphosphorus chloride and di-β-octyl hydrogen phosphite (3·0 g.), b. p. 130—133°/1—2 mm., $\alpha_D^{18°}$ +4·8°, $n_D^{18°}$ 1·4400 (Found: Cl, 3·7%), from which, after washing with water, (+)di-β-octyl hydrogen phosphite (2·5 g.), b. p. 138—140°/2 mm., $\alpha_D^{18°}$ +15·8°, $n_D^{18°}$ 1·4375, $d_4^{18°}$ 0·9176, was obtained; (iv) residue (0·7 g.).

Procedure 1, carried out with the alcohol (3·0 g.) and the trichloride (4·0 g.) in ethereal solution, gave (−)-β-octyloxyphosphorus dichloride (4·0 g.), b. p. 75—76°/1 mm., 119—119·5°/18 mm., $n_D^{16°}$ 1·4666, $\alpha_D^{16°}$ −33·8° (Found: Cl, 30·6%), as main product, no β-octyl chloride being isolated (see Houssa and Phillips, *loc. cit.*).

(−)Phenylmethylcarbinol (Houssa and Kenyon, J., 1930, 2260) ($\alpha_D^{16°}$ −40·3°, 6·1 g., 1 mol.) and the trichloride (13·75 g., 2 mols.) gave a cloudy liquid, which, after being for 1 hour at 15 mm., was poured on ice. After the ethereal extract had been washed with a solution of sodium carbonate, it yielded (+)-α-chloroethylbenzene (5·3 g.), b. p. 78°/15 mm., $\alpha_D^{18°}$ +20·2°, $n_D^{14°}$ 1·5314 (Found: Cl, 25·0. Calc.: Cl, 25·2%), and an undistilled residue (0·61 g.). The carbonate solution gave an oil (0·05 g.) on acidification. (+)-α-Chloroethylbenzene (4·4 g.), $\alpha_D^{18°}$ +19·9°, a residue (0·5 g.), and, from the carbonate solution, a turbid oil (1·0 g.) [Found: P, 14·2. $P(OH)_3{\cdot}OC_8H_9$ requires P, 16·7%] were obtained when 1 mol. of trichloride was used and the product worked up immediately after mixing. It appears, therefore, that the chloride was formed during the actual mixing at low temperature. McKenzie and Clough (J., 1913, **103**, 687) obtained a 54% yield of (+)-α-chloroethylbenzene, α_D +5·9°, by adding the (−)alcohol, α_D −32·0°, to large excess of the trichloride and fractionating the product without its having previously been washed with water. Kenyon, Phillips, and Taylor (J., 1931, 382) obtained a 17·5% yield of (+)-α-chloroethylbenzene, α_{5461} +10·0°, by adding the (−)alcohol, α_{5461} −52·4°, to excess of the trichloride in ethereal solution, with potassium carbonate in suspension, and distilling the product without aqueous treatment.

Ethyl (−)mandelate was obtained by resolution of mandelic acid by means of *l*-ephedrine (Manske and Johnson, *J. Amer. Chem. Soc.*, 1929, **51**, 1909), followed by esterification by the benzene–alcohol–water ternary mixture method. Owing to the large amount of material required, specimens of mandelate which fell a little short of optical purity had to be used.

The (−)mandelate ($\alpha_D^{16°}$ −131·0°, 9 g., 1 mol.) and the trichloride (13·75 g., 2 mols.) gave a product which attained almost constant weight (14·6 g.) after being in a vacuum for 7½ hours (the theoretical weight for $PCl_2{\cdot}OR$ is 14·05 g.). It then had $\alpha_D^{16°}$ −122·9°, $n_D^{18°}$ 1·5277 (Found: Cl, readily hydrolysed, 26·3; P, 11·5. $C_{16}H_{14}O_3Cl_2P$ requires Cl, 25·2; P, 11·0%), being (−)-*α-carbethoxybenzyloxyphosphorus dichloride*, $PCl_2{\cdot}O{\cdot}CHPh{\cdot}CO_2Et$. (i) 6·8 G. of this product, after being kept at 100°/15 mm. for 1 hour, had $\alpha_D^{16°}$ −136·4°, and as its temperature was raised slowly from 100° to 190° it gave a distillate (0·7 g.), b. p. 138—140°/14 mm., $\alpha_D^{16°}$ −14·8°, $n_D^{16°}$ 1·5200. (ii) 6·8 G. of the product were poured on ice, and the ethereal

extract, after being washed with a solution of sodium carbonate, gave a colourless liquid (1·4 g.), $\alpha_D^{16°}$ −50·7°, containing only a trace of chlorine. From the carbonate solution a thick gum (4·15 g.) (Found: P, 11·0%) was obtained.

The product (16·9 g. after 2 hours and 16·0 g. after 3 hours at 15 mm.) obtained from (−)mandelate (9 g.) and trichloride (13·8 g.) was kept for 7 days at 18° and then for 2 hours at 18°/15 mm. It still weighed 16·0 g. and had $\alpha_D^{18°}$ −114·2° (Found: Cl, readily hydrolysed, 29·0%). (i) 5·0 G. of the product were poured on ice. From the ethereal solution, after extraction with a solution of sodium carbonate, a liquid (0·6 g.) (not distilled), $\alpha_D^{18°}$ −55·0°, $n_D^{18°}$ 1·5140 (Found: Cl, 4·1%), was obtained. The carbonate solution gave a viscous residue (1·6 g.), $\alpha_D^{18°}$ −114·0° [Found: P, 11·9. The *dihydrogen phosphite*, $P(OH)_2{\cdot}O{\cdot}CHPh{\cdot}CO_2Et$, $C_{10}H_{13}O_5P$, requires P, 12·7%). (ii) 4·0 G. of the original product, heated at 100°/754 mm. for 1·5 hours, then at 100°/15 mm. for 45 minutes, had $\alpha_D^{18°}$ −129·6° (Found: Cl, readily hydrolysed, 21·3%). From the ethereal solution of this, after extraction with a solution of sodium carbonate, a residue (0·5 g.) (Found: Cl, 4·2%) was obtained. The carbonate solution gave as before a viscous residue (1·2 g.), $\alpha_D^{18°}$ −114·3° (Found: P, 12·0%).

It may be concluded from these experiments (*a*) that the chlorophosphite is formed in some quantity, but (*b*) it does not decompose (or ionise) to give ethyl phenylchloroacetate; and (*c*) that there is no clue to the mechanism of formation of the small amount of the chloroacetate which appears to be present.

Finally, the (−)mandelate (8·2 g.) and trichloride (11·7 g.) by Procedure (1) gave a product, which, after 1 hour at 50° and ½ hour at 100°/15 mm., had $\alpha_D^{18°}$ −136·8°, and on fractionation yielded a liquid (3·5 g.), b. p. 105—108°/2 mm., $d_4^{19°}$ 1·2827, $d_4^{21°}$ 1·2720, $n_D^{21°}$ 1·5259, $\alpha_D^{18°}$ −117·5° (Found: Cl, 25·1; P, 10·6%), and a residue of thick gum (4·4 g.).

Procedure (2). *Addition of Phosphorus Trichloride to the Hydroxy-compound.*—Procedure (1) was followed, but with reversed order of addition.

(+)-α-Octanol (4·3 g., 1 mol.) and the trichloride (1·6 g., 0·33 mol.) evolved hydrogen chloride (0·76 g.) during mixing, and on distillation yielded (−)-β-octyl chloride (1·6 g.), b. p. 60—62°/13 mm., $\alpha_D^{18°}$ −29·0°, $n_D^{18°}$ 1·4273, and a residue, which appeared to be a mixture of the di- (1·5 g.) and the mono-octyl phosphite (0·5 g.). In a second experiment with the alcohol (3·2 g.) and trichloride (1·2 g.), hydrogen chloride (0·46 g.) was evolved, and the residue (3·9 g., after being at 15 mm. for 1 hour), was poured into water. After the ethereal extract had been washed with a solution of sodium carbonate, it gave (−)-β-octyl chloride (1·0 g.), b. p. 64°/19 mm., $\alpha_D^{18°}$ −30·4°, $n_D^{18°}$ 1·4275 (Found: Cl, 23·8. Calc.: Cl, 23·9%), and (+)di-β-octyl hydrogen phosphite (2·2 g.), b. p. 135—138°/2 mm., $\alpha_D^{18°}$ +15·8°, $n_D^{18°}$ 1·4370, $d_4^{18°}$ 0·9177 (Found: P, 10·1. Calc.: P, 10·1%). Acidification of the carbonate extract yielded only 0·1 g. of an oil. These results support the scheme $3ROH + PCl_3 \longrightarrow RCl + P(OR)_2{\cdot}OH + 2HCl$.

(−)Phenylmethylcarbinol ($\alpha_D^{16°}$ −40·3°, 3·05 g., 1 mol.) and the trichloride (1·2 g., 0·33 mol.) gave a turbid liquid, the ethereal solution of which, after being washed with a solution of sodium carbonate, yielded (+)-α-chloroethylbenzene (2·05 g.), b. p. 78°/17 mm., $\alpha_D^{22°}$ +19·9°, $n_D^{25°}$ 1·5272 (Found: Cl, 25·0. Calc.: Cl, 25·2%), and a residue (0·7 g.), $\alpha_D^{22°}$ −72·1°, $n_D^{22°}$ 1·5412. The carbonate solution gave but a faint cloudiness on acidification. Essentially the same results were obtained by use of 0·66 mol. or of 1·0 mol. of the trichloride.

Ethyl (−)mandelate (6 g., 1 mol.) and the trichloride (1·6 g., 0·33 mol.) gave a product (6·9 g., after being at 15 mm. for a few minutes), the ethereal solution of which, after being teated with ice and washed with a solution of sodium carbonate, yielded a mixture (1·7 g.) of ethyl (−)mandelate and ethyl (+)phenylchloroacetate b. p. 83—84°/2 mm. (the two substances have similar b. p's.), $\alpha_D^{18°}$ +40·5°, $n_D^{19°}$ 1·5112 (Found: Cl, 12·6. Calc. for the chloroacetate: Cl, 17·9%), and a residue (3·4 g.), $\alpha_D^{18°}$ −93·6°, $n_D^{20°}$ 1·5200 [Found: P, 7·2. (−)*Bis-α-carbethoxybenzyl hydrogen phosphite*, $C_{20}H_{23}O_7P$, requires P, 7·6%]. The carbonate solution deposited an oil (0·3 g.), probably the dihydrogen phosphite, $n_D^{20°}$ 1·5110. Kenyon, Lipscomb, and Phillips (J., 1931, 2275), using 1 mol. of the trichloride and a more rigorous treatment, obtained the chloroacetate (96% RCl), α_{5461} +79·3°, in unstated yield.

Procedure (3). *Addition of Phosphorus Trichloride to the Hydroxy-compound and Pyridine in Ethereal Solution.*—Pyridine hydrochloride was precipitated during the addition of the trichloride in ethereal solution at 0°, the precipitation being complete at the end of the operation. The mixture was filtered rapidly, and the ethereal filtrate evaporated to a residue which was examined as specifically stated.

(−)-β-Octanol ($\alpha_D^{20°}$ −8·0°, 26 g., 1 mol.), pyridine (15·8 g., 1 mol.), and the trichloride (9·2 g., 0·33 mol.) yielded pyridine hydrochloride (22·5 g.) (Found: Cl, 30·3. Calc.: Cl, 30·7%) and a residue (27·5 g.), $\alpha_D^{16°}$ −3·1°, $d_4^{18°}$ 0·8784, $n_D^{16°}$ 1·4432 (Found: P, 7·5%), results in good accord with the scheme $3ROH + 3C_5H_5N + PCl_3 \longrightarrow P(OR)_3 + 3C_5H_5N,HCl$. On distillation, however, the following were obtained: β-octanol (2·0 g.), b. p. up to 88°/18 mm., (−)di-β-octyl hydrogen phosphite (7·5 g.), b. p. 142—144°/2 mm., $\alpha_D^{20°}$ −14·5°, $n_D^{21°}$ 1·4391, $d_4^{21°}$ 0·9133 (Found: P, 10·0. Calc.: P, 10·1%), a mixture of the latter substance and tri-β-octyl phosphite (8·0 g.), b. p. 145—155°/2 mm., $\alpha_D^{20°}$ −8·0°, $n_D^{21°}$ 1·4420, $d_4^{21°}$ 0·8969 (Found: P, 8·7%), which were gradually separated by prolonged fractionation, and (−)*tri-β-octyl phosphite* (8·5 g.), b. p. 162—164°/2 mm., $\alpha_D^{20°}$ −0·8°, $n_D^{22°}$ 1·4449, $d_4^{22°}$ 0·8843 (Found: P, 7·5. $C_{24}H_{51}O_3P$ requires P, 7·4%). Essentially the same results were obtained when pyridine was replaced in turn by quinoline and dimethylaniline.

These results compare with those obtained from the addition of an ethereal solution of (−)-β-octyloxyphosphorus dichloride (5·7 g., 1 mol.), $\alpha_D^{18°}$ −34·2°, from (+)-β-octanol, $\alpha_D^{18°}$ +8·0°, to (+)-β-octanol (6·5 g., 2 mols.) and pyridine (3·95 g., 2 mols.) in ether. Precipitation of pyridine hydrochloride (5·5 g.) (Found: Cl, 30·0. Calc.: Cl, 30·7%) was complete at the end of the addition, and the filtered solution yielded: β-octanol (1·2 g.), b. p. 80—82°/14 mm., $n_D^{18°}$ 1·4271, $\alpha_D^{16°}$ +1·0; the hydrogen phosphite (2·5 g.), b. p. 138—145/2 mm., $\alpha_D^{16°}$ +14·1°, $n_D^{16°}$ 1·4381; the phosphite (3·3 g.), b. p. 159—162°/2 mm., $\alpha_D^{16°}$ +8·4°, $n_D^{16°}$ 1·4415; residue (0·2 g.).

(−)Phenylmethylcarbinol ($\alpha_D^{22°}$ −41·1°, 7·32 g., 1 mol.), pyridine (4·75 g., 1 mol.), and the trichloride (2·75 g., 0·33 mol.) gave pyridine hydrochloride (7·17 g. Calc.: 6·93 g.) (Found: Cl, 29·2%), all the chlorine thus being accounted for, and a residue (6·7 g.) obtained by evaporation, finally for 3 hours in a vacuum, of the washed and dried ethereal solution (Found: P, 7·8%), $\alpha_D^{18°}$ −65·2°, $n_D^{17°}$ 1·5350, probably mainly the normal phosphite, but it could not be distilled.

Ethyl (+)mandelate ($\alpha_D^{16°}$ +120·1°, 18·0 g., 1 mol.), pyridine (7·9 g., 1 mol.), and the trichloride (4·6 g., 0·33 mol.) gave pyridine hydrochloride (11·3 g. Calc.: 11·6 g.) (Found: Cl, 29·7%), and on evaporation the washed and dried ethereal solution left a residue [16·8 g. Calc. for $P(OR)_3$: 18·9 g.], $\alpha_D^{18°}$ +101·0°, $n_D^{18°}$ 1·5091.

Procedure (4). *Behaviour on Heating the Chlorophosphite with Pyridine or with Pyridine Hydrochloride.*—(−)-β-Octyloxyphosphorus dichloride ($\alpha_D^{18°}$ −34·2°, 5 g.) in ethereal solution did not evolve heat when treated with pyridine (3·9 g., 2 mols.) in ether. There was no sign of reaction during 24 hours at 18° and 1 hour at 50°, the ether being allowed to distil, but there was vigorous reaction when the product was poured on ice; some hydrogen chloride escaped, but the wash water contained ⅞ of the chlorine in the system. The ethereal extract after being washed with a solution of sodium carbonate gave a residue (0·52 g.), $n_D^{23°}$ 1·4378, $\alpha_D^{16°}$ +10·1°, and acidification of the carbonate solution yielded (+)-β-octyl dihydrogen phosphite (2·9 g.), $\alpha_D^{16°}$ +5·0°, $n_D^{16°}$ 1·4388 (Found: P, 15·7. Calc.: P, 16·0%). The dichloride (3 g.), heated with pyridine (2 g.) in absence of ether for 2 hours at 70—80° and worked up as in the preceding experiment, yielded, from carbonate-washed ether, 0·05 g. of residue and from the carbonate solution afforded (+)-β-octyl dihydrogen phosphite (1·8 g.), $\alpha_D^{16°}$ +5·8°, $d_4^{15°}$ 1·0210, $d_4^{20°}$ 0·9913 (Found: P, 16·0. Calc.: P, 16·0%). Heating the chlorophosphite with pyridine hydrochloride gave essentially the same results.

Procedure (5). *Addition of Phosphorus Trichloride to the Phosphite.*—(−)Tri-β-octyl phosphite (5·9 g., 1 mol.), $\alpha_D^{18°}$

$-0{\cdot}8°$, from (−)-β-octanol, $\alpha_D^{18°}$ $-18{\cdot}0°$, was treated with the trichloride (4 g., 2 mols.) at 0°. Two hours after the mixing, the liquid had $\alpha_D^{20°}$ $+4{\cdot}8°$, unchanged after 24 hours' standing at 20°. After being at 20°/15 mm. for 2 hrs. and at 30°/15 mm. for 1 hr., the product (8·1 g.) (Found: Cl, readily hydrolysed, 26·6%) was treated as follows. (i) 3·5 G., heated at 100° for 1 hour, poured on ice, and extracted with ether gave, after the latter had been washed with a solution of sodium carbonate, the (−)hydrogen phosphite (0·85 g.), b. p. 136°/2 mm., $\alpha_D^{20°}$ $-14{\cdot}5°$, $n_D^{22°}$ 1·4370. (Found: P, 10·0. Calc.: P, 10·1%), and a residue (0·5 g.). The carbonate solution yielded impure dihydrogen phosphite (0·59 g.) (Found: P, 13·9%). (ii) 3·5 G. mixed with pyridine (1·5 g.) and heated at 100° for 1 hour gave almost exactly the same results, (−)hydrogen phosphite (0·85 g.), $\alpha_D^{18°}$ $-14{\cdot}2°$, $n_D^{20°}$ 1·4385 (Found: P, 9·8%), residue (0·4 g.), and impure dihydrogen phosphite (0·58 g.) (Found: P, 13·8%). It is significant that no β-octyl chloride was formed in these circumstances; an equilibrium mixture of the chlorophosphites appeared to form, and these hydrolysed to the hydrogen and the dihydrogen phosphite.

The "phosphite" product [Procedure (3), (3 g.) from (−)phenylmethylcarbinol, $\alpha_D^{18°}$ $-41{\cdot}1°$] and the trichloride (5 g.) were mixed at 0° and kept for 16 hours at 15°, 2 hours at 15°/15 mm., and finally ½ hour at 70° before being poured on ice. The washed ethereal extract gave (+)-α-chloroethylbenzene (2·5 g.), b. p. 76°/14 mm., $n_D^{17°}$ 1·5302, $\alpha_D^{18°}$ $+36{\cdot}8°$ (Found: Cl, 25·0. Calc.: Cl, 25·2%).

The product (5·6 g.) obtained from ethyl (+)mandelate by procedure (3) was mixed with trichloride (4 g.), and after being in a vacuum for 5 hours the product (8·16 g.) had $\alpha_D^{18°}$ $+115{\cdot}2°$ (Found: Cl, 21·0; P, 11·5%), and yielded on aqueous treatment products which did not contain any chlorine and were too viscous for observation of rotatory power. The residue from the carbonate-washed ether weighed 1·1 g., $n_D^{22°}$ 1·5130; that from the carbonate solution weighed 1·41 g., $n_D^{21°}$ 1·5089 (Found: P, 10·8%).

Procedure (6). *Passage of Hydrogen Chloride through Phosphite.*—(−)Tri-β-octyl phosphite (3·1 g.), [$\alpha_D^{18°}$ 1·1°, from (−)-β-octanol, rapidly absorbed hydrogen chloride at 0—5°, and after aqueous treatment there were obtained (+)-β-octyl chloride (0·65 g.), b. p. 66—67°/20 mm., $\alpha_D^{18°}$ $+20{\cdot}3°$, $n_D^{23°}$ 1·4265; (−)di-β-octyl hydrogen phosphite (1·56 g.), b. p. 133—135°/2 mm., $\alpha_D^{22°}$ $-14{\cdot}8°$ (Found: P, 10·1%), and a residue (0·8 g.).

(−)Di-β-octyl hydrogen phosphite ($\alpha_D^{20°}$ $-14{\cdot}5°$, 3·3 g.) was recovered, except for trace of β-octyl chloride, when hydrogen chloride was passed through it for 3 hours at 15°. After aqueous treatment the (−)hydrogen phosphite (2·3 g.) had b. p. 134—136°/2 mm., $\alpha_D^{22°}$ $-14{\cdot}6°$, $d_4^{21°}$ 0·9177, $n_D^{25°}$ 1·4376 (Found: P, 10·2%). Passage of hydrogen chloride at 50° for 1 hour yielded after aqueous treatment (+)-β-octyl chloride (0·7 g.), b. p. 63°/17 mm., $\alpha_D^{18°}$ $+19{\cdot}9°$, unchanged hydrogen phosphite (0·86 g.), b. p. 123°/1 mm., $\alpha_D^{18°}$ $-14{\cdot}8°$, $n_D^{15°}$ 1·4388 (Found: P, 9·6%), and, from the carbonate extract of the ethereal solution, impure dihydrogen phosphite (0·8 g.) (Found: P, 12·2%).

Procedure (7). *Addition of the Hydroxy-compound to Thionyl Chloride.*—Evidence of the formation of β-octyl chlorosulphinate and α-carbethoxybenzyl chlorosulphinate has already been given (Gerrard, *loc. cit.*), but uncertain results were obtained for phenylmethylcarbinol. The difficulty lies in the complete removal of the excess thionyl chloride before the chlorosulphinate (if formed) decomposes, and in spite of many experiments it can only be assumed that α-phenylethyl chlorosulphinate if formed at all has but transitory existence.

Procedure (7) was conducted as for procedure (1). (+)-β-Octanol ($\alpha_D^{18°}$ $+8{\cdot}0°$, 6·5 g., 1 mol.) and thionyl chloride (6·0 g., 1 mol.) at 0° evolved hydrogen chloride (nearly 1 mol.) but no sulphur dioxide. After 2 hours at 15°/15 mm., the product had $\alpha_D^{16°}$ $-34{\cdot}2°$. Half of this was poured on ice, and β-octyl chloride (0·3 g.), (+)-β-octanol (0·9 g.), b. p. 78—81°/16 mm., $\alpha_D^{18°}$ $+6{\cdot}3°$, and (−)di-β-octyl sulphite (1·5 g.), b. p. 134—135°/2 mm., $\alpha_D^{16°}$ $-16{\cdot}2°$, $n_D^{14°}$ 1·4450 (Found: SO_2, 20·9. Calc.: SO_2, 20·9%), were obtained. After 12 hours, and then 2 hours at 15°/15 mm., the other half had $\alpha_D^{16°}$ $-33{\cdot}5°$ and on aqueous treatment gave essentially the same products as the first half. With thionyl chloride (2 mols.) and the alcohol (6·5 g., 1 mol.), aqueous treatment applied within one hour after mixing afforded (+)-β-octanol (3·3 g.), b. p. 80—81°/17 mm., $\alpha_D^{16°}$ $+7{\cdot}7°$, and di-β-octyl sulphite (2·6 g.), b. p. 134°/2 mm., $\alpha_D^{16°}$ $-16{\cdot}8°$, $n_D^{14°}$ 1·4451 (Found: SO_2, 20·8%) (cf. Levene and Mikeska, *J. Biol. Chem.*, 1924, **59**, 45).

(−)Phenylmethylcarbinol ($\alpha_D^{16°}$ $-41{\cdot}3°$, 3·0 g., 1 mol.) and thionyl chloride (3·0 g., 1 mol.) gave, during mixing, hydrogen chloride (1·1 g.) and sulphur dioxide (1·4 g.), and the product gave after aqueous treatment (−)-α-chloroethylbenzene (2·8 g.), $\alpha_D^{17°}$ $-50{\cdot}9°$, $n_D^{18°}$ 1·5279 (Found: Cl, 25·0. Calc.: Cl, 25·2%) (cf. McKenzie and Clough, *loc. cit.*).

Ethyl (+)mandelate ($\alpha_D^{18°}$ $+120{\cdot}1°$, 9 g., 1 mol.) and thionyl chloride (6·5 g., 1·1 mols.) gave off hydrogen chloride (1·26 g.) but only a trace of sulphur dioxide during the mixing. After one hour at 15 mm., the product attained constant weight (13·3 g. Calc. for R·O·SOCl: 13·2 g.) and had $\alpha_D^{18°}$ $+97{\cdot}7°$, $n_D^{20°}$ 1·5245 (Found, by cold alkali hydrolysis: Cl, 15·0; SO_2, 19·8. Calc. for R·O·SOCl: Cl, 13·6; SO_2, 24·4%). Although the nature of the material prevents purification, there seems little doubt that the chlorosulphinate was present in quantity. 3·7 G. of the product on aqueous treatment yielded a mixture of ethyl (+)mandelate and the chloroacetate (2·7 g.), b. p. 139—141°/16 mm., $\alpha_D^{20°}$ $+113{\cdot}2°$, $n_D^{19°}$ 1·5144 (Found: Cl, 2·7%). 3·7 G. of the first product, after standing for 12 hours at room temperature and 15 mm., had $\alpha_D^{18°}$ $+89{\cdot}6°$ (Found, cold hydrolysis: Cl, 6·8; SO_2, 12·6%), and after 4 days at room temperature it had $\alpha_D^{18°}$ $+72{\cdot}9°$, $n_D^{20°}$ 1·5075. After aqueous treatment it yielded ethyl (+)phenylchloroacetate (2·6 g.), b. p. 138°/13 mm., $\alpha_D^{18°}$ $+84{\cdot}2°$, $n_D^{19°}$ 1·5150 (Found: Cl, 17·1%) (cf. McKenzie and Barrow, J., 1911, **99**, 1910). 5·0 G. of another specimen when heated to 70° (1 hour) with pyridine hydrochloride (2 g.) yielded, after aqueous treatment, ethyl (−)phenylchloroacetate (3·0 g.), b. p. 137°/12 mm., $\alpha_D^{20°}$ $-5{\cdot}2°$, $n_D^{20°}$ 1·5149 (Found: Cl, 17·8%). 5·0 G. of this second specimen, when treated with pyridine (1·5 g.) in ethereal solution at 15°, yielded impure chloroacetate (1·2 g.), $\alpha_D^{22°}$ 20·1° (Found: Cl, 14·1%), and sulphite (1·5 g.), $\alpha_D^{22°}$ $+110°$ (Found: SO_2, 15·2%).

Procedure (8). *Addition of Thionyl Chloride to the Hydroxy-compounds.*—The operation was the same as in procedure (2). (+)-β-Octanol ($\alpha_D^{18°}$ $+8{\cdot}0°$, 4·1 g., 1 mol.) and thionyl chloride (4 g., 1 mol.) evolved hydrogen chloride (1·85 g.) but no sulphur dioxide. After being for 1 hour at 15°/15 mm., the product gave on aqueous treatment a trace of β-octyl chloride, (+)-β-octanol (1·2 g.), b. p. 77—80°/15 mm., $\alpha_D^{15°}$ $+6{\cdot}8°$, and (−)di-β-octyl sulphite (2·2 g.), b. p. 134°/2 mm., $n_D^{14°}$ 1·4449, $\alpha_D^{16°}$ $-16{\cdot}5°$ (Found: SO_2, 20·8%).

(+)Phenylmethylcarbinol ($\alpha_D^{17°}$ $+20{\cdot}5°$, 4 g., 1 mol.) and thionyl chloride (4 g., 1 mol.) steadily evolved hydrogen chloride and sulphur dioxide (0·025 g.-mol. of each) during mixing. The product was immediately treated with water, and afforded (+)-α-chloroethylbenzene (3·1 g.), b. p. 75—76°/15 mm., $\alpha_D^{18°}$ $+14{\cdot}6°$, $n_D^{18°}$ 1·5278 (Found: Cl, 24·9%). Repetition with the alcohol (3 g.), mixed with pyridine hydrochloride (2 g.), and thionyl chloride (3 g.) caused during mixing a steady evolution of hydrogen chloride (1·01 g. Calc.: 0·91 g.) and sulphur dioxide (1·04 g. Calc.: 1·6 g.). (Pyridine hydrochloride appears to retain sulphur dioxide.) The product, after aqueous treatment, gave (+)-α-chloroethylbenzene (3·2 g.), b. p. 75—76°/15 mm., $\alpha_D^{17°}$ $+11{\cdot}9°$, $n_D^{18°}$ 1·5289 (Found: Cl, 25·0%).

Ethyl (+)mandelate ($\alpha_D^{18°}$ $+120{\cdot}1°$, 4·5 g., 1 mol.) and thionyl chloride (1·5 g., 0·5 mol.), gave hydrogen chloride (0·52 g.) and a residue which after 2 hours at 15 mm. had $\alpha_D^{20°}$ $+114{\cdot}1°$, $n_D^{22°}$ 1·5218, and on aqueous treatment gave impure chloroacetate (2·6 g.), b. p. 138—139°/14 mm., $\alpha_D^{24°}$ $+92{\cdot}6°$, $n_D^{24°}$ 1·5120 (Found: Cl, 13·6%), and a residue (1·2 g.), probably α-carbethoxybenzyl sulphite, b. p. 215—225°/2 mm. (slight decomp.) (Found: SO_2, 15·0%).

Procedure (9). *Addition of Thionyl Chloride to the Hydroxy-compound in Presence of Pyridine.*—The details are the same as for Procedure (3). (−)-β-Octanol ($\alpha_D^{20°}$ $-8{\cdot}1°$, 26·0 g., 2 mols.), pyridine (15·8 g., 2 mols.), and thionyl chloride (11·9 g., 1 mol.), all in ethereal solution, yielded pyridine hydrochloride (23·0 g. Calc.: 23·0 g.) (Found: Cl, 30·5; C_5H_5N, 68·8.

Calc.: Cl, 30·7; C_5H_5N, 68·7%), and from the washed ethereal solution, (+)di-β-octyl sulphite (25·1 g., 84%), b. p. 128—129°/1 mm., $\alpha_D^{26°}$ +18·0°, $d_4^{18°}$ 0·9275, $n_D^{22°}$ 1·4436 (Found: S, 10·5. Calc.: S, 10·5%). Hunter (J., 1924, **125**, 1389) prepared (−)di-β-octyl sulphite, $\alpha_{5890}^{17°}$ −18·43°, by addition of thionyl chloride to (+)-β-octanol in petroleum, followed by distillation without aqueous treatment.

With (+)phenylmethylcarbinol ($\alpha_D^{18°}$ +20·3°, 12·2 g., 1 mol.), pyridine (8·0 g., 1 mol.), and thionyl chloride (9 g., 0·75 mol.) in ether an entirely different result was obtained. The (−)-α-chloroethylbenzene was formed during the actual addition, it being necessary to use 0·75 mol. of thionyl chloride to effect complete precipitation of pyridine. Furthermore, there was no evidence that di-α-phenylethyl sulphite was formed at all. The white precipitate (12·1 g.) (Found: Cl, 28·2; C_5H_5N, 65·7; SO_3, 4·8%) was filtered off immediately, and the ethereal solution after being washed gave (−)-α-chloroethylbenzene (7·0 g.), b. p. 74°/15 mm., $\alpha_D^{18°}$ −22·4°, $n_D^{15°}$ 1·5300 (Found: Cl, 25·0%), and a residue (oil-bath, 160°) (3·5 g.), $\alpha_D^{18°}$ +69·6°, which did not respond to the usual analysis of sulphites but yet with thionyl chloride gave (+)-α-chloroethylbenzene (2·4 g.), b. p. 78—80°/18 mm., $\alpha_D^{18°}$ + 20·5°. In another experiment procedure (9) gave, from (−)alcohol, $\alpha_D^{18°}$ −37·2°, (+)-α-chloroethylbenzene, $\alpha_D^{18°}$ +41·6°. In a previous experiment on inactive material, already reported, this peculiar behaviour was not detected, for difficulty was experienced in handling the precipitate, attributed to a solvent action of the "sulphite," and so the precipitate was assumed to be pyridine hydrochloride. The residual ethereal solution was not worked up, but was treated with more thionyl chloride, the action of which was assumed to be the formation of the chloroethylbenzene from the sulphite.

It is noteworthy that, whereas addition of (+)phenylmethylcarbinol to excess acetyl chloride led to formation of α-chloroethylbenzene with almost entire loss of activity (McKenzie and Clough, *loc. cit.*), yet it is now found that the (+)alcohol ($\alpha_D^{18°}$ +9·4°, 4·07 g., 1 mol.) and pyridine (2·63 g., 1 mol.), in ethereal solution, treated with acetyl chloride (2·6 g., 1 mol.) gave little but (+)-α-phenylethyl acetate (3·55 g.), b. p. 99°/13 mm., $\alpha_D^{18°}$ +18·0°. Furthermore, addition of ethyl chlorosulphinate (8·7 g., 1 mol.) to an ethereal solution of (−)phenylmethylcarbinol ($\alpha_D^{18°}$ −37·2°, 8·1 g., 1 mol.) and pyridine (5·27 g., 1 mol.) yielded pyridine hydrochloride (7·3 g. Calc.: 7·6 g.) (Found: Cl, 30·4%) and (−)-*α-phenylethyl ethyl sulphite* (88% yield), b. p. 93°/2—3 mm., $\alpha_D^{20°}$ −94·5° (Found: SO_3, 29·5. $C_{10}H_{14}O_3S$ requires SO_3, 29·9%).

Ethyl (+)mandelate ($\alpha_D^{18°}$ +120·3°, 9 g., 1 mol.), pyridine (4 g., 1 mol.), and thionyl chloride (3 g., 0·5 mol.) yielded pyridine hydrochloride (5·75 g. Calc.: 5·75 g.) (Found: Cl, 30·3%), and a residue (8·8 g., from the washed ethereal solution), $\alpha_D^{18°}$ +124·2°, $n_D^{26°}$ 1·5237. A small portion of this was distilled, b. p. 218—221°/2 mm., $\alpha_D^{22°}$ +124·1°, $n_D^{24°}$ 1·5272 [Found: SO_3 15·4. (+)*Bis-α-carbethoxybenzyl sulphite*, $C_{20}H_{22}O_7S$, requires SO_3, 15·8%].

Procedure (10). *Addition of Thionyl Chloride to Sulphite.*—(+)Di-β-octyl sulphite ($\alpha_D^{22°}$ +18·0°, 7·61 g., 1 mol.) and thionyl chloride (3·0 g., 1 mol.) were kept together at 22°. The mixture attained maximum rotation after 10 hours: 0 hr., +15·4°; 1 hr., 19·9°; 2 hrs., 24·1°; 4 hrs., 29·3°; 5 hrs., 30·8°; 6 hrs., 32·0°; 9 hrs., 33·2°; 10 hrs., +33·4°. After aqueous treatment, the following fractions were obtained: (+)-β-octyl chloride (0·9 g.), b. p. 64—67°/18 mm., $\alpha_D^{18°}$ +5·9°, $n_D^{19°}$ 1·4260; (−)-β-octanol (1·8 g.), b. p. 78—81°/18 mm., $\alpha_D^{19°}$ −0·6°, $n_D^{19°}$ 1·4268; and (+)di-β-octyl sulphite (3·6 g.), b. p. 185°/18 mm., $\alpha_D^{19°}$ +13·7°, $n_D^{20°}$ 1·4435 (Found: S, 10·40. Calc.: S, 10·46%). From this it appears that an equilibrium mixture of thionyl chloride, chlorosulphinate, and sulphite was formed. Another specimen of this mixture from 4 g. of sulphite gave with pyridine (2 g.) in ethereal solution a dark-red oil (about 1 g.; Gerrard, *loc. cit.*), and from the ether, (+)-β-octyl chloride (2·5 g.), b. p. 64°/19 mm., $n_D^{22°}$ 1·4259, $\alpha_D^{20°}$ +25·6°, was obtained.

(−)-α-Phenylethyl ethyl sulphite [3·2 g., 1 mol., $\alpha_D^{20°}$ −94·5°, from (−)-alcohol, $\alpha_D^{20°}$ −37·2°], used in place of di-α-phenylethyl sulphite which could not be obtained in the usual way, and thionyl chloride (1·8 g., 1 mol.) were mixed at 0°, and after 7 hours at 15°, the product was poured on ice. (−)-α-Chloroethylbenzene (1·9 g.), b. p. 85°/25 mm., $\alpha_D^{25°}$ −45·7°, $n_D^{25°}$ 1·5260 (Found: Cl, 25·0%), was isolated. Thionyl chloride (1·8 g., 1 mol.) added to a mixture of (−)sulphite (3·2 g.) and pyridine (2·4 g., 2 mols.) yielded, without being heated, (+)-α-chloroethylbenzene (0·6 g.), b. p. 85°/25 mm., $\alpha_D^{20°}$ +2·4° (Found: Cl, 24·9%).

(+)Bis-α-carbethoxybenzyl sulphite (5·5 g.), $\alpha_D^{18°}$ +124·2°, from (+)mandelate, $\alpha_D^{18°}$ +120·1°, and thionyl chloride (2·5 g.), after standing for 5 days at 17°, had $\alpha_D^{13°}$ +56·5° and had liberated sulphur dioxide (0·7 g.). One half of the product gave after aqueous treatment ethyl (+)phenylchloroacetate (1·5 g.), b. p. 137°/12 mm., $\alpha_D^{20°}$ +75·6, $n_D^{20°}$ 1·5146 (Found: Cl, 17·6%), and a residue (0·8 g.) of sulphite. The other half, after being heated at 100° for 2 hours, and then given aqueous treatment, yielded (+)chloroacetate (2·0 g.), b. p. 137°/12 mm., $\alpha_D^{20°}$ +76·2°, $n_D^{20°}$ 1·5149 (Found: Cl, 17·9%), and a residue (0·3 g.) of sulphite. Thionyl chloride (1·5 g., 0·5 mol.) was added to an ethereal solution of (+)mandelate (4·5 g., 1 mol., $\alpha_D^{18°}$ +120·1°) and pyridine (2 g., 1 mol.). To the mixture of sulphite and pyridine hydrochloride which remained when the ether was evaporated, thionyl chloride (1·5 g., 0·5 mol.) was added, and the product heated at 80° for 2 hours. Ether extraction left a white solid (2·8 g., theoretical for pyridine hydrochloride) and on aqueous treatment the ethereal solution yielded (−)chloroacetate (3·5 g.), b. p. 138°/13 mm., $n_D^{19°}$ 1·5147, $\alpha_D^{18°}$ −35·0° (Found: Cl, 17·8%). Kenyon, Lipscomb, and Phillips (J., 1930, 415) heated the ethereal solution for 30 mins. and got a product containing 63% of chloroacetate (Cl, 11·3%). The presence of ethyl mandelate in this product was due, not to its failure to react, but to the hydrolysis of the chlorosulphinate which under the conditions (pyridine hydrochloride as a separate phase) had not decomposed.

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34. *The Elimination of Bromide Ion from Aqueous Solutions of Phenylbromoacetic Acid.*

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The rate at which bromide ion is liberated from aqueous solutions of phenylbromoacetic acid has been studied in the presence of nitric acid up to a concentration of 1·0M. The course of the reaction is satisfactorily accounted for by a general equation in terms of the acidity of the solution, but under suitable conditions simpler equations are applicable.

The dissociation constant of phenylbromoacetic acid in the presence of M-sodium nitrate has been determined by kinetic measurements and is $6·1 \times 10^{-3}$ at 25°.

It is shown that the reactivity of the undissociated phenylbromoacetic acid cannot be greater than about 0·002 of that of the phenylbromoacetate ion.

In a previous paper (Bulcraig and Dawson, J., 1943, 80) observations on the hydrolysis of the group $CHPhBr{\cdot}CO_2$ in alkaline and in neutral solutions were reported. Consideration of the kinetic measurements leads to the conclusion that under these conditions the only process leading to the elimination of bromide ion is one involving the phenylbromoacetate ion. In particular, even in the absence of any added alkali, the course of the reaction is completely accounted for on the basis of the reactivity of the anion, although in the later stages of the reaction, considerable proportions of undissociated phenylbromoacetic acid are present in the solution. It follows, therefore, in agreement with Senter and Tucker (J., 1916, **109**, 690), that the reactivity of the undissociated acid must be very small in comparison with that of the ion, and consequently, it is only in solutions of relatively high acidity that the reactivity of the acid itself would be revealed. The kinetic measurements now described refer to the rate of liberation of bromide ion from phenylbromoacetic acid at 25° in the presence of various concentrations of nitric acid under controlled conditions of electrolyte content, and the analysis of the observations is based initially on the tentative assumption that the ion only is undergoing reaction. As in previous papers, concentrations are in g.-mols./l. and time is in minutes.

In the presence of added nitric acid, as in an initially neutral solution, the course of the reaction as followed by the rate of production of bromide ion will not, in general, conform to the simple unimolecular formula, owing to the increase in acidity during the reaction, and indeed, it is not possible to derive any simple rate expression of a general nature in terms of the directly measured quantities. On the other hand, however, it is possible to obtain an equation of general applicability in terms of the acidity of the solution. The derivation of this equation is given below, since Senter's equation (J., 1915, **107**, 908), which refers to an analogous system, is but a special case of the general expression. If a and b are respectively the initial concentrations of phenylbromoacetic acid and of nitric acid, and x and y are respectively the concentrations of bromide ions and hydrions at any instant, then, account being taken of the processes

$$CHPhBr{\cdot}CO_2H \rightleftarrows CHPhBr{\cdot}\bar{C}O_2 + \overset{+}{H}$$

and

$$CHPhBr{\cdot}\bar{C}O_2 \rightarrow \bar{Br} + \text{reaction products}$$

it follows that $a = [CHPhBr{\cdot}CO_2H] + [CHPhBr{\cdot}\bar{C}O_2] + x$ and, if the contribution to the acidity made by the reaction products is neglected,

$$y = [CHPhBr{\cdot}\bar{C}O_2] + b + x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Hence, since

$$K = [H^+][CHPhBr{\cdot}\bar{C}O_2]/[CHPhBr{\cdot}CO_2H] = y(y - b - x)/(a + b - y) \quad . \quad . \quad . \quad (2)$$

then

$$x = y - b + K - K(a + b)/y$$

and

$$dx/dy = 1 + K(a + b)/y^2$$

If only the phenylbromoacetate ion is reacting

$$dx/dt = k_2[CHPhBr{\cdot}\bar{C}O_2] = k_2(y - b - x)$$

and consequently

$$dy/dt = (dy/dx)(dx/dt) = k_2y^2(y - b - x)/[y^2 + (a + b)K] = k_2Ky(a + b - y)/[y^2 + (a + b)K]$$

which on integration gives

$$k_2 = \frac{1}{Kt}\left\{K \ln \frac{y}{y_0} - (a + b + K) \ln \frac{a + b - y}{a + b - y_0} + y_0 - y\right\} \quad . \quad . \quad . \quad . \quad (3)$$

where y_0 is the value of y when $t = 0$.

The application of equation (3) to the experimental data, which is shown in Table I, involves the tedious calculation from each value of x of the corresponding value of y, by means of the equation

$$y = \tfrac{1}{2}\left\{x + b - K + \sqrt{(K - x - b)^2 + 4K(a + b)}\right\}$$

For this reason a series of equations in terms of x have been developed, which are more convenient to handle, although each of these equations, in contrast to equation (3), is valid over only a restricted range of acidities. It follows from (1) and (2) that

$$[CHPhBr{\cdot}\bar{C}O_2] = K(a - x)/(K + b + x + [CHPhBr{\cdot}\bar{C}O_2]).$$

Now when $b =$ or $> a$, $b > [CHPhBr{\cdot}\bar{C}O_2]$, and hence as a first approximation,

$$K + b + x + [CHPhBr{\cdot}\bar{C}O_2] = K + b + x + K(a - x)/(K + b + x)$$

from which it follows that

$$[CHPhBr{\cdot}\bar{C}O_2] = K(a - x)(K + b + x)/[(K + b + x)^2 + K(a - x)]$$

Hence

$$dx/dt = k_4K(a - x)(K + b + x)/[(K + b + x)^2 + K(a - x)]$$

which on integration gives

$$k_4 = \frac{1}{t}\left\{\frac{a + b + K}{K}\ln\frac{a}{a - x} + \ln\frac{K + b + x}{K + b} - \frac{x}{K}\right\} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

When b is much greater than a, a further simplification is possible, for it may then be assumed that

$$[CHPhBr{\cdot}\bar{C}O_2] = K(a - x)/(K + b + x)$$

from which it follows that

$$k_5 = \frac{1}{t}\left\{\frac{a + b + K}{K}\ln\frac{a}{a - x} - \frac{x}{K}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Finally, when b is very large, equation (5) reduces to the pseudo-unimolecular formula

$$k_6 = [(a + b + K)/Kt]\ln a/(a - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

The evaluation of the velocity coefficient of the reaction by means of equations (3)—(6) involves a knowledge of the dissociation constant of phenylbromoacetic acid. The recorded value of this constant at 25° is $3{\cdot}5 \times 10^{-3}$ (Senter and Tucker, *loc. cit.*) but this was determined by means of conductivity measurements on the acid solution which was undergoing hydrolysis, and moreover, it relates to a dilute aqueous solution of the acid, so it is not only suspect but is also not applicable to the strong salt solutions used in the present experiments. It has therefore been necessary, by means of kinetic experiments, to determine the dissociation constant of the acid under the prevailing salt conditions. The velocity measurements used for this purpose refer to solutions of low acidity, where, as already pointed out, it is evident that only the phenylbromoacetate ion undergoes reaction. Equation (3) alone is valid under these conditions. The application of this equation, together with a knowledge of k_3, as evaluated from measurements in alkaline solutions (Bulcraig and Dawson, *loc. cit.*), then allows of the determination of K. The data for two experiments are given in (*a*) and (*b*) of Table I. In each case, in the second line are given the bromide-ion concentrations (x), as determined by silver titration, and in the third line the hydrion concentrations (y) derived therefrom on the assumption that $K = 6{\cdot}06 \times 10^{-3}$ in (*a*) and $6{\cdot}15 \times 10^{-3}$ in (*b*); these numbers lead to the previously determined value for 10^4k_3, *viz.*, 207. The approximate constancy of the values of k_3, given in the last line, shows that the premises on which the calculation is based are substantially correct. It may therefore be taken that K has the value $6{\cdot}1 \times 10^{-3}$ in these solutions, and this value has been adopted in all subsequent experiments.

TABLE I.

(*a*) 0·025M-CHPhBr·CO_2H + 1·0M-$NaNO_3$; $K = 6{\cdot}06 \times 10^{-3}$.

t	0	30	45	60	85	100	122	150	180	240
10^3x	0	4·63	6·67	8·33	10·68	12·00	13·42	15·03	16·57	18·58
10^3y	9·68	11·65	12·65	13·53	14·85	15·66	16·55	17·61	18·65	20·08
10^4k_3	—	204	208	208	205	210	206	207	207	205

(*b*) 0·025M-CHPhBr·CO_2H + 0·01M-HNO_3 + 0·99M-$NaNO_3$; $K = 6{\cdot}15 \times 10^{-3}$.

t	0	15	30	45	60	90	121	150	180	210	270	360
10^3x	0	1·47	3·18	4·76	6·17	8·62	10·74	12·52	13·86	15·08	16·96	19·21
10^3y	16·71	17·55	18·59	19·58	20·50	22·17	23·67	24·98	25·99	26·92	28·39	30·19
10^4k_3	—	—	206	204	204	205	207	211	208	207	205	206

Two series of experiments were carried out. In the first series (A) where the solutions were of composition 0·025M-CHPhBr·CO_2H + bM-HNO_3 + $(1 - b)$M-$NaNO_3$, the total electrolyte concentration remained constant at 1 g.-mol./l. In the second series (B) a constant concentration of sodium nitrate was maintained, the solutions having compositions given by 0·025M-CHPhBr·CO_2H + bM-HNO_3 + 1·0M-$NaNO_3$. In such solutions, as b is progressively increased, equations (4), (5), and (6) become successively applicable. When $b =$ or $>0{\cdot}025$, equation (4) accounts satisfactorily for the course of the reaction, as is shown by the constancy of the coefficients given in the last line of Table II (*a*) as an example.

TABLE II.

(*a*) 0·025M-CHPhBr·CO_2H + 0·050M-HNO_3 + 1·0M-$NaNO_3$.

t	30	60	100	160	240	300	420	550	660
$\ln 10^3(b + K + x)/(b + K)$	24	50	80	116	158	182	222	255	276
$[(a + b + K)/K]\ln a/(a - x)$	0·75	1·61	2·73	4·31	6·40	7·87	10·86	13·97	16·61
$10^3x/K$	224	469	759	1134	1564	1830	2284	2662	2924
10^4k_4	210	213	213	211	212	210	211	212	213

(*b*) 0·025M-CHPhBr·CO_2H + 1·0M-HNO_3.

t	782	1445	2287	2920	3700	5100	6670	9450
10^3x	2·872	4·961	7·452	9·036	10·90	13·57	15·93	19·05
$[(a + b + K)/K]\ln a/(a - x)$	20·52	37·27	59·62	75·56	96·47	131·8	170·8	241·8
x/K	0·47	0·81	1·22	1·48	1·78	2·22	2·60	3·11
10^4k_5	256	252	255	254	256	254	252	253
10^4k_6	268	263	266	264	266	264	262	262

When $b \ll$ *ca.* 0·2, equation (5) becomes applicable, and when b has reached 1·0, the course of the reaction approximates to the pseudo-unimolecular. In the last two lines of Table II(b) are given the coefficients as calculated from equations (5) and (6) respectively. For this reaction mixture it will be noted that, although the course of the reaction is accounted for by a pseudo-unimolecular formula, the resulting coefficients are considerably greater than the true values obtained by means of equation (5).

The results given above are typical of those obtained throughout the experiments, and the remainder are therefore given in summarised form. In Table III, section A (cols. 2, 3, 4) and section B (col. 5), are given respectively the velocity coefficients for the first and the second series of experiments. Section C is discussed later. Inspection of the figures in sections A and B shows that the value of k_4 remains constant over only a

TABLE III.

0·025M-CHPhBr·CO_2H + bM-HNO_3 with added $NaNO_3$.

	A.			B.	C.		A.			B.	C.
	[$NaNO_3$] = 1 − b.			[$NaNO_3$] = 1.			[$NaNO_3$] = 1 − b.			[$NaNO_3$] = 1.	
b.	10^4k_3.	10^4k_4.	10^4k_5.	10^4k_4.	$10^4k_{corr.}$.	b.	10^4k_3.	10^4k_4.	10^4k_5.	10^4k_4.	$10^4k_{corr.}$.
0	205	—	—	—	—	0·200	—	214	213	222	220
0·0100	207	—	—	—	—	0·300	—	221	221	228	230
0·0250	—	206	—	—	—	0·500	—	232	232	240	247
0·0500	—	207	—	211	209	1·00	—	254	254	266	285
0·100	—	209	—	213	212						

limited range of b values, and thereafter increases steadily with increase in b. Since k is derived on the assumption that only the phenylbromoacetate ion is undergoing hydrolysis, the increase in k in solutions of high acidity might be taken as indicating that under these conditions the hydrolysis of the undissociated acid is no longer negligible in comparison with that of the ion. It is shown below, however, that such a conclusion does not necessarily follow if due regard is paid to the possible influence of other factors.

In this connection it will be noted that in section A, where the total concentration of electrolyte remains practically constant throughout the series, there is a gradual replacement of sodium nitrate by nitric acid as b increases, whereas in section B the total electrolyte content of the solution increases continuously with the addition of nitric acid. Hence, in both cases, account must be taken of the possibility that the velocity of reaction will be modified by intervention of inert-salt effects. These effects may be expected to be two-fold: (i) there is the primary salt effect which influences the velocity of reaction directly, and (ii), since the apparent specific reaction rate is here a function of the equilibrium constant K, account must also be taken of the possible secondary salt effect.

Evidence as to the magnitude of the primary salt effect is provided by the figures given below, which refer to conditions under which secondary salt effects can play no part (Bulcraig and Dawson, *loc. cit.*). The numbers given in the last line of the table are obtained by means of the equation $10^4k_{calc.} = 181 + 31C$. It is thus clear

0·025M-CHPhBr·CO_2Na + 0·050M-NaOH + CM-$NaNO_3$.

C	0	0·425	0·925	1·425	1·925
$10^4k_{obs.}$	180	195	207	225	242
$10^4k_{calc.}$	181	194	210	224	241

that the primary salt effect is linear up to an ionic strength, μ, of about 2·0. The systematic differences which are found between the velocity coefficients for corresponding solutions in series A and B must be due, at least in part, to the primary salt effect of sodium nitrate, since the compositions of the two series of solutions differ only in respect of sodium nitrate content. On the basis of the above data an allowance for this difference in primary salt effect can be made. The correction is made by adding to each of the velocity coefficients given in Table III,A the quantity 31Δ[$NaNO_3$], where Δ[$NaNO_3$] is the difference in sodium nitrate concentration between corresponding solutions (*i.e.*, identical b values) in the two series. The resulting values of $k_{corr.}$ are given in section C of Table III. A comparison of these numbers with the corresponding ones in section B shows that the two are in substantial agreement up to a value for b of nearly 0·5. It may be recalled that the velocity coefficients are a function of K, from which it is apparent that the agreement noted above implies that K has the same value in both series A and B; *i.e.*, the secondary salt effects do not differ appreciably in the two series. If it is borne in mind that as between the two series of solutions very considerable differences in total electrolyte concentration may exist, it becomes clear that, in the range of high electrolyte concentrations employed in these experiments, the value of K is relatively insensitive to quite large changes in ionic environment. The assumption of a constant value for K appears, therefore, to be amply justified over the greater part of the concentration range.

This conclusion is also suggested by the evidence recorded by Dawson and Lowson (J., 1929, 1217) and it is pertinent that in the presence of a sufficiently large concentration of electrolyte, K will decrease with the addition of further electrolyte. It might reasonably be supposed that this stage is reached when μ has attained the value of 2·0, as in the last experiment in series B. The velocity coefficient for this mixture ($10^4k = 266$) is appreciably smaller than that for the corresponding solution in series A ($10^4k_{corr.} = 285$). It seems probable that this difference is due to a decrease in K in the solution of higher electrolyte content.

From the foregoing discussion it is clear that, with the exception of the solutions just noted, the increase in k with increase in concentration of nitric acid is real, and is therefore due either to the hydrolysis of the acid itself or to the primary salt effect on the specific reaction rate of the ion, brought about by the gradual increase in nitric acid concentration. If the latter be the case, the results given in B and C of Table III would require that the salt effect due to nitric acid should be about 2·6 times that due to sodium nitrate. No data on this point are available, but the figures given below for the effect on k of four different electrolytes (sodium salts or hydroxide) show the strongly specific nature of these effects:

Electrolyte.	Nitrate.	Perchlorate.	Hydroxide.	Mandelate.
Increase, %, in k for 0·925M-electrolyte	15·0	26·1	12·2	6·7

In view of these figures it would clearly be unsafe to reject the possibility that the observed changes in k are due entirely to the primary salt effect of the nitric acid and that the phenylbromoacetic acid is completely unreactive. It is therefore not possible to give a definite value for the specific velocity for the undissociated acid. On the other hand, a reliable estimate can be made of the maximum value that this coefficient can have.

The minimum value that can be assigned to the primary salt effect caused by nitric acid is obviously zero. On this supposition the increases in k in B and C of Table III will represent partial velocities due to the hydrolysis of the phenylbromoacetic acid. These partial velocities (Δk) are given in l. 3 of Table IV and are in each case the difference between the observed velocity coefficient (mean of values under B and C) and that for the phenylbromoacetate ion which is 207×10^{-4}.

TABLE IV.

0·025M-CHPhBr·CO_2H + bM-HNO_3 + 1M-$NaNO_3$.

b	0·050	0·100	0·200	0·300	0·500
$10^4k_{obs.}$	210	213	221	229	244
$10^4\Delta k$	3	6	14	22	37
$[H^+]$	—	0·11	0·21	0·31	0·51
10^5k	—	3·3	4·1	4·3	4·4

The values for the specific velocity for the acid, k_m, are then obtained from $k_m = \Delta k/[\text{CHPhBr·CO}_2\text{H}] = \Delta k \cdot K/[H^+]$ on taking for $[H^+]$ the mean of the initial and the final value for each experiment. The maximum value for k_m is thus about 4×10^{-5}. It can, therefore, be asserted that the reactivity of phenylbromoacetic acid, if indeed this is admitted at all, cannot be greater than about 0·002 of that of the phenylbromoacetate ion.

Experimental.—The reaction was started by dissolving the phenylbromoacetic acid in the appropriate aqueous solution, and followed by estimating the liberated bromide, as previously described. In the absence of free alkali the dissolution of the acid is slow and hence it is not possible to assess directly an exact time for the commencement of the reaction. This was obtained as follows. For each of the velocity equations a straight line is obtained when a function of x or y is plotted against time. The intercept of the line on the time axis gives the error in the estimated zero time which is used in making the plot. This correction, which is usually 1—4 minutes, is added or substracted to give the true zero time of the reaction.

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35. *Analogues of Pantothenic Acid. Part IV. Aryl Derivatives of Pantoyltaurine.*

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Three aryl-substituted analogues of pantoyltaurine (I) have been prepared, in an attempt to make antibacterial substances which would be growth-inhibitors by virtue of their structural relationship to pantothenic acid, but which would be less water-soluble than pantoyltaurine and so possibly have a higher *in vivo* activity. The new analogues are β-(αγ-dihydroxy-ββ-dimethylbutyramido)-α-phenylethanesulphonic acid (II), β-(αγ-dihydroxy-ββ-diphenylbutyramido)ethanesulphonic acid (III), and β-(α-tosyl-γ-hydroxy-ββ-dimethylbutyramido)-ethanesulphonic acid (IV). None of these shows bacteriostatic activity *in vitro* or *in vivo*.

THE preparation of analogues of pantothenic acid possessing growth-inhibiting properties, by virtue of their structural relationship to pantothenic acid, has so far been limited to the aliphatic series (Part II, Barnett and Robinson, *Biochem. J.*, 1942, **36**, 364; Part III, Barnett, this vol., p. 5). *N*-Pantoyltaurine (I), the sulphonic acid analogue of pantothenic acid, has been found highly active in inhibiting the growth *in vitro* of micro-organisms for which pantothenic acid is essential (McIlwain, *Biochem. J.*, 1942, **36**, 417; *Brit. J. exp. Path.*, 1942, **23**, 95; Snell, *J. Biol. Chem.*, 1941, **139**, 975; **141**, 121; Kuhn *et al.*, *Ber.*, 1941, **74**, 1605), but has an effect *in vivo* only in very high doses (McIlwain and Hawking, *Lancet*, 1943, **i**, 449). This is due, in part, to the extremely high rate of excretion of pantoyltaurine, making it difficult to maintain a bacteriostatic concentration in the blood, and, on the other hand, to the presence in the animal organism of pantothenic acid, which antagonises the effect of pantoyltaurine.

With the object of reducing the solubility of pantoyltaurine and, at the same time, preserving as far as

possible the structural relationship to pantothenic acid, two phenyl derivatives of pantoyltaurine were synthesised. It was hoped by this means to reduce the rate of excretion and yet to retain antibacterial activity. These two substances, β-(αγ-dihydroxy-ββ-dimethylbutyramido)-α-phenylethanesulphonic acid (II) and β-(αγ-dihydroxy-ββ-diphenylbutyramido)ethanesulphonic acid (III), were almost inactive *in vitro* against *Lactobacillus arabinosus*. As might have been expected, (II) was inactive *in vivo*; (III) was not tested.

A different method of reducing the rate of excretion was also tried. This involved introducing a toluenesulphonyl group on the α-hydroxy-group of pantoyltaurine to give β-(α-tosyl-γ-hydroxy-ββ-dimethylbutyramido)-ethanesulphonic acid. It was expected that this compound would have no *in vitro* activity, but would slowly hydrolyse in the body, giving pantoyltaurine; it was, however, inactive both *in vitro* and *in vivo*.

(I.) $CH_2(OH)\cdot CMe_2\cdot CH(OH)\cdot CO\cdot NH\cdot CH_2\cdot CH_2\cdot SO_3H$ $CH_2(OH)\cdot CMe_2\cdot CH(OH)\cdot CO\cdot NH\cdot CH_2\cdot CHPh\cdot SO_3H$ (II.)

(III.) $CH_2(OH)\cdot CPh_2\cdot CH(OH)\cdot CO\cdot NH\cdot CH_2\cdot CH_2\cdot SO_3H$ $CH_2(OH)\cdot CMe_2\cdot CH(OTs)\cdot CO\cdot NH\cdot CH_2\cdot CH_2\cdot SO_3H$ (IV.)

where Ts = toluene-*p*-sulphonyl.

Compound (II) was prepared as follows: catalytic reduction of *iso*nitrosoacetophenone by means of palladised charcoal gave phenylethanolamine (Hartung *et al.*, *J. Amer. Chem. Soc.*, 1928, **50**, 3370; 1930, **52**, 3317; 1931, **53**, 2248, 4149) in 49% yield. This reacted with thionyl chloride at room temperature to give β-phenyl-β-chloroethylamine hydrochloride in 66% yield; the method is more convenient than that of Wolfheim (*Ber.*, 1914, **47**, 1466). The compound was converted into *α-phenyltaurine* in 40% yield by prolonged heating with sodium sulphite solution. The *sodium* salt of α-phenyltaurine was condensed with pantolactone to give (II). dl-*α-Hydroxy-ββ-diphenyl-γ-butyrolactone*, the substance required for the preparation of (III), was synthesised by a method analogous to that used for the preparation of pantolactone. Ethoxyacetic ester (*Org. Synth.*, 1933, **13**, 42) was converted, by means of a Grignard reaction, into diphenylethoxymethylcarbinol by Béhal and Sommelet's method (*Compt. rend.*, 1904, **138**, 89); this, on heating with oxalic acid (Danilov *et al.*, *Ber.*, 1926, **59**, 1032), gave diphenylacetaldehyde. This was condensed with formaldehyde by means of solid potassium carbonate. The reaction was not quantitative, however, as after a short time the mixture set to a solid mass in spite of vigorous shaking, occluding large amounts of starting material. Attempts to avoid this by carrying out a condensation in alcohol or ether were unsuccessful. The crude product was condensed with anhydrous hydrogen cyanide in ether containing a drop of piperidine. The resulting cyanohydrin was hydrolysed, giving the required butyrolactone. This was obtained in two forms, m. p. 141° and 175—176°; the one could not be converted into the other by seeding and neither form gave an amide or a phenylhydrazide.

The lack of reactivity of the lactone is consistent with the difficulty of condensing it with taurine. Various conditions for the condensation were tried, including fusion in the dry state, but in no instance did the reaction proceed to an extent greater than 50%, the best yield being obtained by refluxing in methyl-alcoholic solution for 15 hours.

The preparation of a third phenyl analogue of pantoyltaurine, namely, (α-hydroxy-β-phenyl-ββ-dimethylpropionamido)ethanesulphonic acid, had been planned, and for this purpose *α-hydroxy-β-phenylisovaleric acid* was prepared, but in view of the negative results with the above compounds, the preparation of this analogue was not completed. α-Hydroxy-β-phenyl*iso*valeric acid was prepared from phenyl*iso*butaldehyde obtained by Tiffeneau and Dorlencourt's method (*Ann. Chim. Phys.*, 1907, **10**, 247). Some difficulty was encountered, however, in preparing the cyanohydrin, since phenyl*iso*butaldehyde does not form a bisulphite compound. The condensation was therefore attempted with potassium cyanide in presence of calcium chloride (Reichstein, *Helv. Chim. Acta*, 1940, **23**, 650; Carter and Ney, *J. Amer. Chem. Soc.*, 1941, **63**, 313), but no reaction took place. Eventually the cyanohydrin was obtained by the action of anhydrous hydrogen cyanide and a drop of piperidine, but even by this method the yield of acid after hydrolysis of the cyanohydrin was only 24%.

β-(α-Tosyl-γ-hydroxy-ββ-dimethylbutyramido)ethanesulphonic acid (IV) was obtained as its *sodium* salt by the condensation of the sodium salt of taurine with *α-tosyl-ββ-dimethylbutyrolactone* (*monotosylpantolactone*) in methyl-alcoholic solution in the usual way. The monotosyl lactone was obtained in 76% yield by treatment of pantolactone in pyridine solution with tosyl chloride.

Compound (II), tested *in vitro* on *Streptococcus hæmolyticus* strain 618, showed no antibacterial activity in dilutions of from 1 : 1000 to 1 : 500,000. It was also practically inactive against *Lactobacillus arabinosus in vitro*. *In vivo* tests on rats indicated that the substance afforded no protection against *Streptococcus hæmolyticus*, the latter being recovered from their organs. Control animals, given substance (II) but not infected, remained healthy. Compound (III) also was practically inactive *in vitro* against *Lactobacillus arabinosus*, in concentrations at which pantoyltaurine inhibited growth. Compound (IV) was inactive *in vitro* against *Lactobacillus arabinosus* and against *Streptococcus hæmolyticus*, and *in vivo* it had no protective action in mice and rats infected with *Streptococcus hæmolyticus*. All the animals died during treatment and *Streptococcus hæmolyticus* was recoverable from their organs.

Experimental.

α-Phenyltaurine.—Thionyl chloride (13·5 ml.) in absolute benzene (15 ml.) was added slowly with stirring to β-phenyl-β-hydroxyethylamine hydrochloride (24 g.). When the mixture showed signs of becoming viscous, a further 10 ml. of benzene were added, and the whole was shaken thoroughly. After 12 hours, the mixture was distilled in a vacuum at 50° (bath temp.) to remove volatile products, the residue taken up in alcohol, and β-phenyl-β-chloroethylamine hydrochloride precipitated with ether (yield, 22·5 g.) and recrystallised from ethyl alcohol, giving 14 g., m. p. 157—158°.

A mixture of β-phenyl-β-chloroethylamine hydrochloride (8·4 g.), sodium sulphite (12·3 g.), and water (150 ml.)

was heated under reflux on the steam-bath for 18 hours and then evaporated to dryness in an open dish. A solution of the solid in the minimum amount of boiling water was filtered hot; on cooling, *α-phenyltaurine* (3·8 g.) crystallised in white platelets, m. p. 258° (decomp.); it gave a negative test for halogen. The mother-liquor was treated with concentrated hydrochloric acid, filtered from sodium chloride, and treated with acetone; the α-phenyltaurine thereby obtained had m. p. 258° after recrystallisation from hot water (yield, 0·5 g.). Total yield, 40% (Found: C, 47·9; H, 5·25; N, 6·7; S, 16·1. $C_8H_{11}O_3NS$ requires C, 47·8; H, 5·5; N, 6·9; S, 15·9%).

The *sodium* salt was prepared by addition of sodium hydroxide (1 equiv.) to an aqueous solution of α-phenyltaurine, followed by evaporation to dryness in a vacuum and removal of traces of water by means of alcohol and absolute toluene. A white powder was obtained which was almost non-hygroscopic (Found: N, 5·6; S, 14·2; Na, 10·1. $C_8H_{10}O_3NSNa$ requires N, 6·2; S, 14·3; Na, 10·3%).

Sodium β-(αγ-Dihydroxy-ββ-dimethylbutyramido)-α-phenylethanesulphonate (as II).—The sodium salt of α-phenyltaurine (3·82 g.) was added to a solution of pantolactone (2·5 g.) in absolute methyl alcohol (30 ml.), which was then refluxed for 6 hours with exclusion of moisture. After cooling and filtration, the solution was concentrated in a vacuum at 40° to small bulk and the syrup obtained was poured into absolute ether with shaking. The granular white precipitate was collected, washed with ether (care being taken to keep it covered with ether), and dried in a vacuum over phosphoric oxide. Yield, 6·4 g. (theor., 6·3 g.) (Found: N, 4·1; S, 8·3; Na, 6·6. $C_{14}H_{29}O_6NSNa$ requires N, 4·0; S, 9·1; Na, 6·5%). It was very hygroscopic, and readily soluble in water.

β-Hydroxy-αα-diphenylpropaldehyde.—To a mixture of diphenylacetaldehyde (10 g., b. p. 170—172°/12 mm.) and 40% formalin solution (4 g.) at 0°, potassium carbonate (2·4 g.) in water (20 ml.) was added gradually with shaking, the reactants being kept cold by ice–salt. The mixture thickened after 5 minutes, and became semi-solid after ½ hour at room temperature. It was warmed at 50° for a few minutes until it was fluid and was then shaken and left at 20° overnight. The aqueous layer was decanted; the solid mass, after being shaken with a little ether, yielded *ca.* 3·8 g., m. p. *ca.* 95°, and was used for the subsequent condensation. It could be recrystallised from alcohol to give material, m. p. 137—139°.

dl-*α-Hydroxy-ββ-diphenyl-γ-butyrolactone.*—(a) *Lactone, m. p.* 141°. β-Hydroxy-αα-diphenylpropaldehyde (700 mg.) was suspended in sodium-dried ether (25 ml.), and a drop of piperidine added, followed by hydrogen cyanide (500 mg.). After 42 hours' shaking, the ether was evaporated, and the residual cyanohydrin refluxed with concentrated hydrochloric acid (10 ml.) for 8 hours. The hydrolysis mixture was extracted three times with ether, the extracts washed with dilute sodium bicarbonate solution (until the washings were alkaline) and with water and dried (sodium sulphate), and the ether distilled. The brownish residue, crystallised twice from benzene after filtering through charcoal, yielded the *lactone* (120 mg.), m. p. 141° (Found: C, 75·4; H, 5·7. $C_{16}H_{14}O_3$ requires C, 75·5; H, 5·55%).

(b) *Lactone, m. p.* 174°. The reaction was carried out on about ten times the scale of the previous experiment, the only difference being that there still remained some undissolved material after 4 days' shaking; this was removed and washed with ether. The washings were added to the filtrate, and the insoluble matter was re-treated with hydrogen cyanide and piperidine, until, after a further day's shaking, it had all dissolved. On working up as before, several crops of crystalline lactone were obtained; this, after being decolorised with charcoal and recrystallised from benzene, yielded the lactone in needles (1·5 g.) m. p. 172—174°. Two more recrystallisations raised the m. p. to 175—176° (Found: C, 75·0; H, 5·7%).

β-(αγ-Dihydroxy-ββ-diphenylbutyramido)ethanesulphonic Acid (III).—*dl*-α-Hydroxy-ββ-diphenyl-γ-butyrolactone (173 mg., m. p. 174—176°) (10% excess) and the sodium salt (90 mg.) of taurine were refluxed in absolute methyl-alcoholic solution (3 ml.) for 15 hours. Absolute ether was added to the cooled concentrated solution, and the precipitate collected rapidly (yield of powder dried over phosphoric oxide, 120 mg.). From the ethereal filtrate unchanged lactone was recovered, m. p. 175—176° after recrystallisation from benzene–petroleum (yield 75 mg.). The mother-liquors yielded a further 12 mg., m. p. 171—173°; the total weight recovered (87 mg.) indicates 55% condensation. A Van Slyke determination gave 2·5% of free amino-nitrogen, which represents 51% condensation.

α-Hydroxy-β-phenylisovaleric Acid.—(*a*) Phenyl*iso*butaldehyde (5 g., b. p. 98—101°/12 mm.) was treated at 0° with anhydrous hydrogen cyanide (1·1 g.; 20% excess) and a drop of piperidine. The mixture was allowed slowly to attain room temperature, concentrated hydrochloric acid (20 ml.) added after 4 days, and the liquid refluxed for 9 hours. Two layers persisted throughout. After being made alkaline, the mixture was extracted twice with ether to remove unchanged phenyl*iso*butaldehyde. It was then acidified with hydrochloric acid and extracted three times with ether; the extracts were washed with a little water and dried, and the ether removed. The residue formed a crystalline cake, which, after two recrystallisations from benzene–light petroleum, yielded α-hydroxy-β-phenyl*iso*valeric acid (670 mg.), m. p. 91—92°.

(*b*) The reactants were mixed exactly as under (*a*) and left at room temperature for 3 weeks; the product was then hydrolysed and worked up as above. The yield of *α-hydroxy-β-phenylisovaleric acid* (1·55 g.), m. p. 94—95° after recrystallisation from benzene–light petroleum, was 24% (Found: C, 68·2; H, 7·3. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%).

Monotosyl Ester of Pantolactone.—A solution of dry redistilled pantolactone (3 g.) in absolute pyridine (10 ml.) was cooled in ice, and an ice-cold solution of toluene-*p*-sulphonyl chloride (5·7 g.) in pyridine (20 ml.) added slowly, with exclusion of moisture. After being left at room temperature for 16 hours, the mixture was heated at 100° for 1 hour, cooled, and poured into ice-cold dilute hydrochloric acid. An oil separated and solidified on stirring. It was collected, washed with water, and dissolved in chloroform. The chloroform solution was washed successively with dilute hydrochloric acid, dilute sodium bicarbonate solution, and water, the washings being extracted twice more with small amounts of chloroform. The extracts, after drying over anhydrous sodium sulphate, were evaporated in a vacuum to dryness. On addition of methyl alcohol to the residue, crystals (4·4 g.) were at once obtained, m. p. 113—114°. A second crop (0·75 g.) from the mother-liquor, after charcoal treatment, had m. p. 113—115°. Recrystallisation from methyl alcohol gave pure *monotosylpantolactone* in white needles, m. p. 114—115° (Found: C, 55·1; H, 6·0; S, 10·6. $C_{13}H_{16}O_5S$ requires C, 54·9; H, 5·7; S, 11·3%).

Sodium β-(α-Tosyl-γ-hydroxy-ββ-dimethylbutyramido)ethanesulphonate (*as* IV).—Monotosylpantolactone (1·42 g.) and the sodium salt (0·73 g.) of taurine were refluxed in absolute methyl alcohol (12 ml.) for 5 hours with exclusion of moisture. The practically clear solution was filtered and worked up as described for (II). Yield, 1·5 g. (71%) of a white hygroscopic powder, from ether (Found: N, 3·7; S, 13·9; Na, 6·5. $C_{15}H_{22}O_8NS_2Na$ requires N, 3·3; S, 14·8; Na, 5·4%). Van Slyke determination of free amino-nitrogen showed 0·86%, indicating 77% condensation.

Melting points are all uncorrected.

Biological tests were carried out in the Department of Experimental Medicine of Glaxo Laboratories Ltd., under the direction of Dr. J. Ungar, and also by Dr. H. McIlwain (Department of Bacterial Chemistry, Medical Research Council), to whom the authors wish to express their indebtedness.

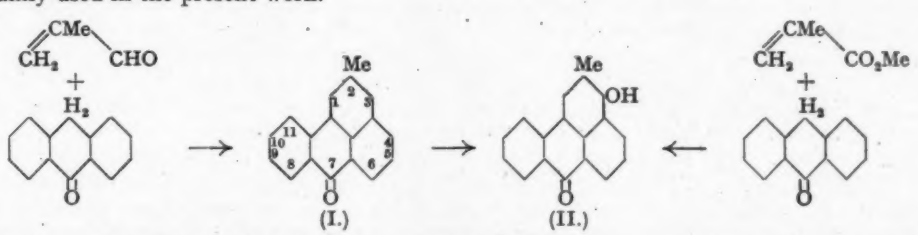
GLAXO LABORATORIES LTD., GREENFORD. [*Received, October 14th*, 1943.]

36. 2-*Methyl*meso*benzanthrone and Some Derivatives.*

By D. H. Hey, R. J. Nicholls, and C. W. Pritchett.

Various methods for the preparation of α-methylacraldehyde are described and 2-methyl*meso*benzanthrone is prepared from this aldehyde or its acetal and anthrone. 2-Methyl*meso*benzanthrone is converted by standard methods into 16 : 17-dimethyldibenzanthrone and 6 : 15-dimethyl*iso*benzanthrone. 3-Hydroxy-2-methyl-*meso*benzanthrone is formed as a by-product in the conversion of 2-methyl*meso*benzanthrone into 2 : 2′-dimethyl-3 : 3′-dibenzanthronyl and the same compound is also obtained from 2-methyl*meso*benzanthrone by nitration, reduction and the diazo-reaction, as well as from the condensation of anthrone with methyl methacrylate. 16 : 17-Dimethyldibenzanthrone is converted in boiling nitrobenzene solution into a product which, it is suggested, contains a new six-membered ring.

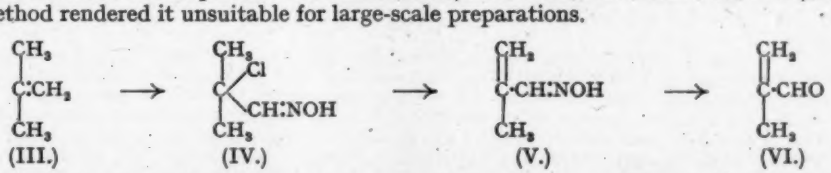
Alkyl*meso*benzanthrones with the substituent group in the benz-ring are prepared by the condensation of an alkyl derivative of glycerol or acraldehyde with anthraquinone or its reduction products, usually in presence of sulphuric acid, following the original method for the preparation of *meso*benzanthrone due to Bally (D.R.-PP. 176,018, 176,019; *Ber.*, 1905, **38**, 194; 1911, **44**, 1656, etc.). Thus the condensation of crotonaldehyde with anthrone yields 1-methyl*meso*benzanthrone * (B.PP. 244,120, 261,400; Baddar and Warren, J., 1939, 944), whereas 3-methyl*meso*benzanthrone is obtained from hydroxymethyleneacetone and anthrone (F.P. 631,995; compare also Liebermann, *Annalen*, 1882, **212**, 96, 120, and Liebermann and Roka, *Ber.*, 1908, **41**, 1423). The comparative difficulty of obtaining suitable β-substituted derivatives of glycerol (cf. Hearne and De Jong, *Ind. Eng. Chem.*, 1941, **33**, 940) has rendered 2-alkyl*meso*benzanthrone less accessible by this route, but under the influence of aluminium chloride alkyl substituents in the 1- and the 3-position in *meso*benzanthrone migrate to the 2-position (U.S.P. 1,713,591; Baddar and Warren, J., 1939, 948). 2-Methyl-*meso*benzanthrone (I) prepared in this way has been shown by the latter authors to be identical with the compound prepared by the condensation of β-methylglycerol αγ-diethyl ether with anthraquinone and also with that obtained by the method of Lüttringhaus and Grosskinsky (B.P. 286,602; D.R.-P. 482,839) from the condensation of α-methylacraldehyde (a derivative of β-methylglycerol) or its acetal with anthrone. The latter aldehyde or its acetal was prepared from α-bromo*iso*butaldehyde by the method of Zeisel and Danieck (*Monatsh.*, 1909, **30**, 727), but the possibility of α-methylallyl alcohol becoming readily available, which can be oxidised to α-methylacraldehyde, renders this condensation more attractive. This method, with various modifications, has been mainly used in the present work.



(I.) (II.)

The oxidation of α-methylallyl alcohol to α-methylacraldehyde was carried out by means of selenium dioxide in dioxan suspension (B.P. 457,174; D.R.-P. 634,501). Condensations with anthrone were carried out with freshly prepared material, since, unless stabilised by the addition of a trace of quinol, the aldehyde readily polymerises to an opaque solid mass. Consistent yields of 2-methyl*meso*benzanthrone (I) of the order of 50—60% were obtained by this method.

Owing to a temporary shortage of supplies of α-methylallyl alcohol, possible alternative synthetic routes to α-methylacraldehyde were investigated. For instance, the diethyl acetal of α-methylacraldehyde, prepared according to the method of Kinney and Adams (*J. Amer. Chem. Soc.*, 1937, **59**, 897), gave on acid hydrolysis the free aldehyde. For the preparation of 2-methyl*meso*benzanthrone the acetal was used. Further, addition of nitrosyl chloride to *iso*butylene (III) gave α-chloro*iso*butaldoxime (IV), which by removal of hydrogen chloride gave the oxime of α-methylacraldehyde (V), from which the free aldehyde (VI) was best generated by treatment with sodium nitrite in presence of acetic acid (cf. Harries, *Ber.*, 1901, **34**, 1494), but the over-all yield by this method rendered it unsuitable for large-scale preparations.



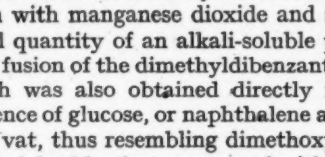
(III.) (IV.) (V.) (VI.)

In another attempt dimethylethynylcarbinol and tetramethylbutynediol were prepared from acetone and acetylene by the methods of Campbell, Campbell, and Eby (*J. Amer. Chem. Soc.*, 1938, **60**, 2882; see also *Organic Syntheses*, 1940, **20**, 40), Bruson and Kroeger (*J. Amer. Chem. Soc.*, 1940, **62**, 41), and Dupont (*Ann. Chim. Phys.*, 1913, **30**, 490), and both were subjected to partial hydrogenation to give dimethylvinylcarbinol

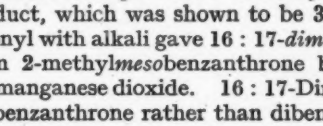
* The method of numbering the *meso*benzanthrone and related systems is that adopted in the " Ring Index " (Patterson and Capell, 1940).

and tetramethylbutenediol respectively (D.R.-P. 288,271; Ott and Schröter, *Ber.*, 1927, **60**, 624). Both the latter carbinol and the diol were subjected to ozonolysis in the normal manner, but the resulting hydroxyaldehyde could not be dehydrated to give α-methylacraldehyde because of the extreme ease with which it underwent polymerisation (cf. Franke, *Monatsh.*, 1900, **21**, 213, 1127; Levene and Walti, *J. Biol. Chem.*, 1931, **94**, 353; Danilov and Venus-Danilova, *J. Gen. Chem., U.S.S.R.*, 1933, **3**, 559).

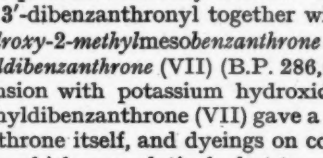
Oxidation of 2-methyl*meso*benzanthrone with chromic acid gave anthraquinone-1-carboxylic acid. Oxidation with manganese dioxide and sulphuric acid gave 2 : 2′-dimethyl-3 : 3′-dibenzanthronyl together with a small quantity of an alkali-soluble product, which was shown to be 3-*hydroxy*-2-*methyl*meso*benzanthrone* (II). Mild fusion of the dimethyldibenzanthronyl with alkali gave 16 : 17-*dimethyldibenzanthrone* (VII) (B.P. 286,602), which was also obtained directly from 2-methyl*meso*benzanthrone by fusion with potassium hydroxide in presence of glucose, or naphthalene and manganese dioxide. 16 : 17-Dimethyldibenzanthrone (VII) gave a deep blue vat, thus resembling dimethoxydibenzanthrone rather than dibenzanthrone itself, and dyeings on cotton were violet-blue but, compared with dibenzanthrone, showed a redder shade which was relatively fast to water-spotting.



(VII.)



(VIII.)



(IX.)

The purification of 16 : 17-dimethyldibenzanthrone (VII) was effected by extraction with boiling *o*-dichlorobenzene, but when boiling nitrobenzene was used as solvent an entirely different product resulted which, while still giving a blue vat, dyed cotton in rather weak dull red shades. This new product did not contain nitrogen and it was found that its formation from the dimethyldibenzanthrone was favoured by the presence of barium oxide. It is tentatively suggested that the rôle of the nitrobenzene in this instance is that of an oxidising agent, the two methyl groups having lost hydrogen with resultant ring closure to give the compound (VIII). This is the more likely since it is already known that 2 : 2′-dimethyl*meso*benzdianthrone is converted into *allomeso*naphthadianthrone under the influence of alkali (B.P. 303,184; D.R.-P. 456,583) : in the present instance traces of alkali may be present from the original fusion.

3-*Chloro*-2-*methyl*meso*benzanthrone* was prepared from 2-methyl*meso*benzanthrone and dichloramine-T in acetic acid solution, and when heated in presence of selenium, calcium hydroxide and copper bronze it gave 2 : 2′-dimethyl-3 : 3′-dibenzanthronyl selenide. Fusion of the latter with alkali gave 6 : 15-*dimethyl*iso*dibenzanthrone* (IX), which gave violet-blue dyeings on cotton from a bright blue vat. The same compound was also prepared by the direct alkaline fusion of 3-chloro-2-methyl*meso*benzanthrone.

In the oxidation of *meso*benzanthrone to dibenzanthronyl some 2-hydroxy*meso*benzanthrone is formed as a by-product (Lüttringhaus and Neresheimer, *Annalen*, 1929, **473**, 272), whereas, as recorded above, in the similar oxidation of 2-methyl*meso*benzanthrone (I), the alkali-soluble by-product proved to be 3-hydroxy-2-methyl*meso*benzanthrone (II). The constitution of the latter was proved by the identity of its *methyl* ether with (*a*) the product obtained from 2-methyl*meso*benzanthrone by nitration, reduction, conversion of the 3-*amino*-2-*methyl*meso*benzanthrone* by means of the diazo-reaction into the corresponding hydroxy-compound, and subsequent methylation, and also with (*b*) the product obtained from the condensation of methyl methacrylate with anthrone in presence of sulphuric acid, followed by methylation. The latter condensation would be expected to yield 3-hydroxy-2-methyl*meso*benzanthrone in the same way as acrylic acid and anthrone yield 3-hydroxy*meso*benzanthrone (D.R.-P. 552,269). Like 3-methoxy*meso*benzanthrone, 3-methoxy-2-methyl*meso*benzanthrone dyes cellulose acetate rayon in bright orange shades. Oxidation of 3-*nitro*-2-*methyl*meso*benzanthrone* with chromic acid gave anthraquinone-1-carboxylic acid, thus confirming the entry of the nitro-group into the benz-ring during the nitration of 2-methyl*meso*benzanthrone. Direct bromination of 2-methyl*meso*benzanthrone gave 3-*bromo*-2-*methyl*meso*benzanthrone*, identical with the product obtained from 3-amino-2-methyl*meso*benzanthrone by means of the diazo-reaction.

Experimental.

α-*Methylacraldehyde.*—(*a*) *From methylallyl alcohol* (cf. B.P. 457,174; D.R.-P. 634,501). To a suspension of selenium dioxide (35 g.) in dioxan (80 g.) stirred at 95—100°, α-methylallyl alcohol (45·5 g.) was added dropwise during 2 hours. The α-methylacraldehyde was allowed to distil through a Lapworth column at the same rate as the alcohol was added, the temperature at the head of the column never exceeding 90°. A further quantity of selenium dioxide (5 g.) was introduced after the alcohol had been added. The crude distillate, which contained a high proportion of dioxan, was fractionally distilled and collected between 65° and 85° (25 g.). The b. p. recorded in B.P. 457,174 and D.R.-P. 634,501 is 68—69°, and B.P. 286,602 and D.R.-P. 482,839 record the b. p. as "about 90°": Shriner and Sharp (*J. Amer. Chem. Soc.*, 1940, **62**, 2245) record b. p. 73·5° and Hearne, Tamele, and Converse (*Ind. Eng. Chem.*, 1941, **33**, 805), b. p. 68·4°. This product was sufficiently pure for use in the preparation of 2-methyl*meso*benzanthrone. Further purification resulted in considerable loss of material. The 2 : 4-dinitrophenylhydrazone, prepared in the usual manner, crystallised from ethyl acetate in small red needles, m. p. 202° (decomp.), and the semicarbazone separated from methyl alcohol in needles, m. p. 194°. Shriner and Sharp (*loc. cit.*) record m. p. 206—206·5° and 197·5—198° for these two derivatives. Attempts to use other solvents (phenetole, anisole, ethyl phthalate and diamyl ether) in the oxidation in place of dioxan gave reduced yields of aldehyde.

(*b*) ***From** α-bromoiso**butaldehyde diethylacetal.*** The acetal of α-bromo*iso*butaldehyde was prepared and converted into α-methylacraldehyde diethyl acetal by the method of Kinney and Adams (*loc. cit.*). Hydrolysis with boiling 10% sulphuric acid liberated the free aldehyde, which was identified by m. p. and mixed m. p. of its 2 : 4-dinitrophenylhydrazone.

(*c*) ***From** iso**butylene.*** *iso*Butylene, prepared by dropping *tert.*-butyl alcohol (100 g.) on to anhydrous oxalic acid (80 g.) at 80° to 90° during 2½ hours and dried (calcium chloride), was passed into a solution of nitrosyl chloride (100 g.) in dry ether (700 c.c.) maintained at −20° to −15°. After standing over-night at −5° to 0°, the α-chloro*iso*butaldoxime (IV) separated in white needles and a further crop was obtained by partial evaporation of the green ethereal filtrate in a current of dry air (total yield 33 g., m. p. 103—104°; cf. Tilden and Sudborough, J., 1893, **63**, 479; Ipatieff and Ssolonina, *J. Russ. Phys. Chem. Soc.*, 1901, **33**, 496). Further concentration of the mother-liquor gave only a deep blue oil (65 g.) with a camphor-like odour. A solution of the oxime (20 g.) in ethyl alcohol (150 c.c.) was refluxed for ½ hour with fused potassium acetate (40 g.) and, after filtration from potassium chloride and excess of acetate, the solution was diluted with water and extracted with ether. Distillation of the dried ethereal extract gave a brown oily residue, which yielded *α-methylacraldoxime* (V) as a colourless oil (12 g.), b. p. 65°/14 mm. (Found : N, 16·2. C_4H_7ON requires N, 16·5%). A solution of sodium nitrite (6 g.) in water (22 c.c.) was added dropwise with stirring to a solution of the oxime (5 g.) in glacial acetic acid (25 c.c.) maintained at 60—70°. Stirring was then continued for 15 minutes at the same temperature. Treatment of a portion of the resulting solution with a solution of 2 : 4-dinitrophenylhydrazine in hydrochloric acid gave α-methylacraldehyde 2 : 4-dinitrophenylhydrazone as an orange-red precipitate, which after purification had m. p. 198—199°, undepressed on admixture with an authentic specimen prepared from α-methylallyl alcohol as described above.

2-*Methyl*meso*benzanthrone* (I) (D.R.-P. 482,839).—(*a*) Sulphuric acid (30 g., *d* 1·53) was added to a solution of anthrone (9·7 g., prepared as described in *Organic Syntheses*, Collective Vol. I, p. 52) in glacial acetic acid (97 g.) and to the resulting solution heated at 80°, α-methylacraldehyde (12 g.), diluted with an equal volume of dioxan, was added during 20 minutes with stirring. The reaction mixture was poured slowly into water (1500 c.c.) with stirring. The tarry greenish precipitate was collected, washed with water, and dried. Purification was effected either by trituration with a small volume of acetone, which removed most of the green impurity, followed by several crystallisations from alcohol–acetone, by distillation with superheated steam at 200°, followed by crystallisation from alcohol, or by chromatographic adsorption on alumina from benzene solution (1 kg. of " Birlec " alumina per 20 g. of crude product) and subsequent elution with the same solvent and evaporation. 2-Methyl*meso*benzanthrone was obtained in yellow needles, m. p. 164° (Found : C, 88·3; H, 4·8. Calc. for $C_{18}H_{12}O$: C, 88·5; H, 4·9%). Purification by chromatographic adsorption gave yields of 50—60% calculated on the anthrone used, the alternative methods affording rather smaller yields.

(*b*) α-Methylacraldehyde diethylacetal (12 g.) was added dropwise during 30 minutes with vigorous stirring to a solution of anthrone (9·7 g.) in sulphuric acid (170 g., *d* 1·706) at 60°. The crude yellow solid (10 g.), which separated on pouring into ice-water, was collected, washed, dried, and purified as described above.

Oxidation of 2-*Methyl*meso*benzanthrone.*—A solution of chromic anhydride (5 g.) in 50% acetic acid (25 c.c.) was added during 20 minutes to a hot solution of 2-methyl*meso*benzanthrone (1 g.) in glacial acetic acid (20 c.c.). After heating on the steam-bath for 2 hours, water was added, and the precipitated solid collected, taken up in aqueous ammonia and filtered. Acidification of the filtrate deposited anthraquinone-1-carboxylic acid, which separated from acetic acid in faintly yellow plates, m. p. 285° (decomp.) both alone and on admixture with an authentic specimen prepared from *meso*benzanthrone by the method of Perkin (J., 1920, **117**, 706).

16 : 17-*Dimethyldibenzanthrone* (VII).—(a) Via 2 : 2′-*dimethyl*-3 : 3′-*dibenzanthronyl* (cf. B.P. 286,602 and 430,914). Manganese dioxide (6 g.) was added during 7 hours to a stirred solution of 2-methyl*meso*benzanthrone (10 g.) in 80% sulphuric acid (240 g.) at 0—5°. Stirring was continued for 20 hours, water (16 c.c.) then added, and the mixture poured slowly with stirring into more water (1200 c.c.). Sodium bisulphite was added (6 g.) and the whole boiled, filtered, washed free from acid, and treated with boiling dilute sodium hydroxide solution. After filtration and washing alkali-free, the residue was dried and washed several times with hot toluene to remove unchanged 2-methyl*meso*benzanthrone. Crude 2 : 2′-dimethyl-3 : 3′-dibenzanthronyl (6 g.) was obtained as a greenish powder in 78% yield, which on crystallisation from *o*-dichlorobenzene gave small yellowish needles, m. p. >360°. The purple-blue alkaline washings gave crude 3-hydroxy-2-methyl*meso*benzanthrone (0·4 g.) on acidification (see below). The dimethyldibenzanthronyl (5 g.) was added during 30 minutes to a melt of potassium hydroxide (50 g.) and ethyl alcohol (45 g.) heated at 120—130°. This temperature was maintained for a further 20 minutes with stirring. The deep blue melt was drowned in water and aerated to complete the precipitation of the dye, which was collected, washed with water until free from alkali, and dried. The product (4·7 g.) was further purified by extraction with boiling *o*-dichlorobenzene. 16 : 17-*Dimethyldibenzanthrone* was obtained in minute violet-black crystals (Found : C, 88·8; H, 4·3. $C_{36}H_{20}O_2$ requires C, 89·2; H, 4·1%). With concentrated sulphuric acid it gave a violet coloration.

(b) ***From** 2-**methyl**meso**benzanthrone*** (cf. D.R.-P. 467,697). A mixture of 2-methyl*meso*benzanthrone (10 g.) and glucose (12·5 g.) was added to molten potassium hydroxide (50 g.) at 230—240°, and the whole well stirred. When effervescence had subsided, the melt was poured into water, and the product (6 g.) isolated by aeration, filtration, washing and drying as above. In a second method (cf. B.P. 430,665) fused potassium acetate (2·5 g.) was added to methyl alcohol (2·5 g.) and stirred until substantially dissolved, potassium hydroxide (15 g.) then added, and the whole heated to 125—130°. Molten naphthalene (25 g.) was then added, followed by 2-methyl*meso*benzanthrone (5 g.). The temperature was raised to 140° during 30 minutes and then manganese dioxide (5 g.) was stirred in during 5—10 minutes. Heating was continued up to 215°, and the melt stirred until almost solid owing to volatilisation of naphthalene. After cooling to 80—90°, water was added, and the naphthalene removed with steam. The residual solid was collected, and the excess of manganese dioxide removed by boiling with water (150 c.c.) containing sulphuric acid (15 g.) and sodium bisulphite (3·5 g.). After filtration, washing, drying and extraction with *o*-dichlorobenzene 16 : 17-dimethyldibenzanthrone (4 g.) was obtained as a violet-black powder identical with that described above.

Oxidation of 16 : 17-*Dimethyldibenzanthrone.*—Crude 16 : 17-dimethyldibenzanthrone (5 g.), contained in an extraction thimble held in a copper gauze bucket suspended in the vapour of the solvent from the lower end of the reflux air-condenser, was extracted with boiling nitrobenzene (40 c.c.) for 8 hours. When cold, the precipitated solid was collected and washed with acetone. The dried product (3 g.), obtained as a dark brown powder with a reddish tinge, dyed cotton with a weak dull red shade from a blue vat. A similar product was obtained on refluxing for 2 hours the crude dimethyldibenzanthrone (9·5 g.) with nitrobenzene (200 c.c.) in presence of barium oxide (2 g.). In this case a portion of the product was filtered off on cooling, and the remainder separated when the filtrate was added to an equal volume of ethyl alcohol. The combined products were digested with dilute hydrochloric acid at 60°, filtered, washed with water, and dried (6 g.).

3-*Chloro*-2-*methyl*meso*benzanthrone* (cf. Cahn, Jones, and Simonsen, J., 1933, 444).—Concentrated hydrochloric acid (0·5 c.c.) was added to a solution of 2-methyl*meso*benzanthrone (5 g.) in warm glacial acetic acid (100 c.c.), followed by the addition of dichloroamine-T (2·5 g.) in small portions with agitation. Fine yellow needles began to separate almost immediately. The mixture was then heated on the steam-bath for 15 hours, after which water (100 c.c.) was added.

When cold, the precipitated product was collected and crystallisation from glacial acetic acid gave 3-*chloro*-2-*methyl*meso*benzanthrone* (4 g.) in golden-yellow needles, m. p. 227—228° (Found: C, 77·4; H, 3·9. $C_{18}H_{11}OCl$ requires C, 77·5; H, 4·0%).

6 : 15-*Dimethyl*iso*dibenzanthrone* (IX).—(a) *From* 3-*chloro*-2-*methyl*meso*benzanthrone* (cf. D.R.-PP. 194,252, 467,697). 3-Chloro-2-methyl*meso*benzanthrone (1·5 g.) was stirred into a melt of potassium hydroxide (6·5 g.) and ethyl alcohol (7·5 c.c.) at 140° and the temperature was gradually raised and maintained at 150—155° for ½ hour. The deep blue melt was poured into water (200 c.c.) and after aeration the precipitated dye was collected, washed free from alkali with water, and dried. 6 : 15-*Dimethyl*iso*dibenzanthrone* was obtained in almost quantitative yield as a dark violet powder (Found: C, 88·7; H, 4·3. $C_{36}H_{20}O_2$ requires C, 89·2; H, 4·1%).

(b) Via 2 : 2′-*dimethyl*-3 : 3′-*dibenzanthronyl selenide* (cf. B.PP. 367,462, 435,321). 3-Chloro-2-methyl*meso*benzanthrone (1·5 g.), selenium powder (0·5 g.), calcium hydroxide (0·5 g.), copper bronze (0·5 g.), and ethyl alcohol (25 c.c.) were heated for 60 hours at 200° in a sealed tube. When cold, the product was washed out with alcohol into water (200 c.c.). Hydrochloric acid (0·5 c.c.) was added and, after boiling, the product was collected, washed with water, and dried in an air-oven. Subsequent extraction with boiling nitrobenzene gave 2 : 2′-dimethyl-3 : 3′-dibenzanthronyl selenide (1 g.) as a yellow-brown powder, m. p. 310—315°. The selenide (1·5 g.) was stirred into a melt of potassium hydroxide (4·7 g.) and ethyl alcohol (4 c.c.) at 120° during 15 minutes. The temperature was raised to 130° and after 1½ hours the product was poured into water (40 c.c.). Aqueous sodium bisulphite (1·5 c.c. of 45% solution) was added and, after boiling, the precipitated dye was collected, washed free from alkali, and dried. It was identical in properties with that obtained by method (a).

3-*Nitro*-2-*methyl*meso*benzanthrone* (cf. Lüttringhaus and Neresheimer, *loc. cit.*, p. 285).—Nitric acid (88%; 3 c.c.) was added dropwise to a suspension of finely divided 2-methyl*meso*benzanthrone (5 g.) in nitrobenzene (40 c.c.) at room temperature. A brownish-red solution resulted and the temperature rose spontaneously to 40°. Stirring was continued for 2½ hours at 40—50°, during which time a mass of fine yellow needles separated. When cold, ethyl alcohol (40 c.c.) was added, and the precipitated solid collected, washed with alcohol, and dried (5 g., m. p. 215—217°). Recrystallisation from benzene or glacial acetic acid gave 3-*nitro*-2-*methyl*meso*benzanthrone* (3·6 g.) in orange-yellow needles, m. p. 218—219° (Found: C, 75·0; H, 3·9. $C_{18}H_{11}O_3N$ requires C, 74·8; H, 3·8%). Oxidation of the nitro-compound with chromic acid, as described above for the oxidation of 2-methyl*meso*benzanthrone, gave anthraquinone-1-carboxylic acid, m. p. and mixed m. p. with an authentic specimen 285°.

3-*Amino*-2-*methyl*meso*benzanthrone*.—Finely divided 3-nitro-2-methyl*meso*benzanthrone (3 g.) in suspension in aqueous sodium sulphide (30 c.c.; 15% solution) was stirred for ½ hour at room temperature, and the temperature then raised slowly to boiling. After boiling for 1 hour, the red solid was collected and washed well with water (2·7 g.; m. p. 225—231°). Crystallisation from dilute pyridine gave 3-*amino*-2-*methyl*meso*benzanthrone* (2·2 g.) in bright red needles, m. p. 232° (Found: C, 83·3; H, 5·2. $C_{18}H_{13}ON$ requires C, 83·4; H, 5·0%).

3-*Bromo*-2-*methyl*meso*benzanthrone*.—(a) *From* 2-*methyl*meso*benzanthrone*. A 25% solution of bromine in glacial acetic acid (16 g.) was added dropwise with stirring to a solution of 2-methyl*meso*benzanthrone (5 g.) in glacial acetic acid (80 g.) at 80°. The mixture became pasty, rendering stirring difficult, and the temperature was then raised and maintained at 90—100° until evolution of hydrogen bromide ceased. Water (20 c.c.) was added, and the precipitated solid collected, washed, and dried (4·5 g., m. p. 216—222°). Purification by high-vacuum sublimation or chromatographic adsorption on alumina from benzene solution gave 3-*bromo*-2-*methyl*meso*benzanthrone*, which formed orange-yellow needles, m. p. 225°, from glacial acetic acid (Found: C, 66·7; H, 3·5. $C_{18}H_{11}OBr$ requires C, 66·9; H, 3·4%).

(b) *From* 3-*amino*-2-*methyl*meso*benzanthrone*. A solution of the base (1 g.) in concentrated sulphuric acid (10 c.c.) was diazotised with sodium nitrite (0·3 g.). After ½ hour the solid diazonium sulphate, obtained as a yellowish-brown precipitate when the solution was poured on ice, was added to a solution of cuprous bromide (2 g.) in hydrobromic acid (10 c.c.; *d* 1·45) stirred at room temperature. When evolution of nitrogen had ceased, the mixture was heated on the steam-bath. Dilution with water precipitated the product as a brown solid (1·1 g.). Crystallisation from glacial acetic acid gave 3-bromo-2-methyl*meso*benzanthrone in yellow needles, m. p. 225°, identical with the product prepared by method (a).

3-*Hydroxy*-2-*methyl*meso*benzanthrone* (II).—(a) *From the oxidation of* 2-*methyl*meso*benzanthrone*. The purple-blue alkaline washings obtained in the preparation of 2 : 2′-dimethyl-3 : 3′-dibenzanthronyl described above were acidified with hydrochloric acid, and the resulting orange-brown precipitate collected, washed with water, and dried. Purification was effected by chromatographic adsorption on alumina from benzene containing 10% of ethyl alcohol. The bright purple band was eluted with the same solvent and concentration of the elutriate deposited 3-*hydroxy*-2-*methyl*meso*benzanthrone* in small brick-red needles, m. p. 206—208° (decomp.) (Found: C, 83·0; H, 4·7. $C_{18}H_{12}O_2$ requires C, 83·1; H, 4·6%).

(b) *From methyl methacrylate and anthrone*. Methyl methacrylate (20 g.) was added slowly during ½ hour to a well-stirred solution of anthrone (40 g.) in concentrated sulphuric acid (200 g.) at 70°. After being stirred for 2½ hours at this temperature, the dark-red solution (blue fluorescence) was cooled and poured on ice. The precipitated solid was extracted with aqueous sodium hydroxide, and the filtered dark green solution aerated until the colour had become purple-blue. Acidification with hydrochloric acid deposited an orange-brown precipitate, which was collected, washed, and dried at 50°. Chromatographic adsorption on alumina (1 kg.) was carried out as described above, and the purple band separated mechanically. Elutriation as before gave 3-hydroxy-2-methyl*meso*benzanthrone (3 g.) in small red needles.

(c) *From* 3-*amino*-2-*methyl*meso*benzanthrone*. A solution of 3-amino-2-methyl*meso*benzanthrone (1 g.) in 50% sulphuric acid (20 c.c.) was diazotised with sodium nitrite (0·4 g.). After standing for ½ hour at room temperature, the mixture was diluted with an equal volume of water and heated on the steam-bath. When evolution of nitrogen had ceased, the suspended solid was collected (pump), and dissolved in aqueous sodium hydroxide (purple-blue solution); from the filtered solution, the hydroxy-compound (1 g.) was precipitated with hydrochloric acid.

3-*Methoxy*-2-*methyl*meso*benzanthrone*.—Solutions of 3-hydroxy-2-methyl*meso*benzanthrone (2 g.), prepared by methods (a), (b) and (c) above, in acetone (100 c.c.) were refluxed for 10 hours with methyl iodide (1·2 g.) and anhydrous potassium carbonate (0·6 g.). The solvent was removed by distillation, and the residue boiled with water. The brownish-yellow solid was collected, dissolved in benzene, and purified either chromatographically by adsorption on alumina or by vacuum sublimation. Subsequent crystallisation from benzene–light petroleum (b. p. 40—60°) or dilute methyl alcohol gave in all three cases 3-*methoxy*-2-*methyl*meso*benzanthrone* (2 g.) in lemon-yellow needles, m. p. 142° (Found: C, 83·0; H, 5·4. $C_{19}H_{14}O_2$ requires C, 83·2; H, 5·1%).

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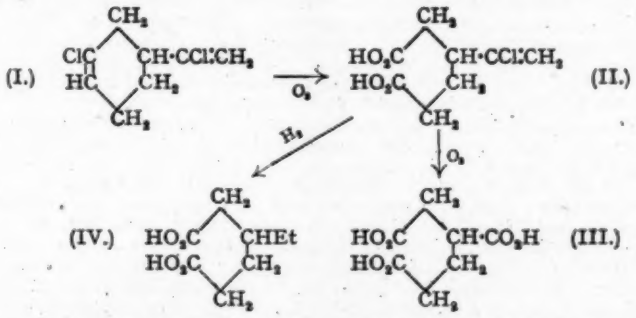
37. 3-*Chloro*-1-α-*chlorovinyl*-Δ³-cyclo*hexene*, *and* 1 : 5-*Dichloro*-Δ¹·⁵-cyclo-*octadiene*.

By J. G. T. Brown, J. D. Rose, and J. L. Simonsen.

The two dimers formed when chloroprene is kept either as such or in a solvent (Carothers, Williams, Collins, and Kirby, *J. Amer. Chem. Soc.*, 1931, **53**, 4211; Carothers, Kirby, and Collins, *ibid.*, 1933, **55**, 791) have been shown to have the structures represented by (I) and (V).

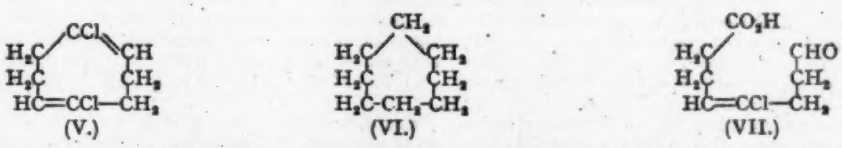
During his investigations on chloroprene, Carothers and his collaborators (*locc. cit.*) observed the formation of a " β-polymer " when chloroprene was kept alone or in a solvent. This polymer can be separated into two fractions, b. p. 92—93°/27 mm. and 114—118°/27 mm. The structure of these polymers was not determined, but, having a quantity available, we have undertaken this, for it seemed that a knowledge of their structure might throw some further light in the mechanism of polymerisation.

Fractionation of the oil remaining after the removal of the monomer and some xylene gave two fractions having approximately the same b. p.'s as those obtained by Carothers. The b. p. and the analytical data indicated that they consisted essentially of two dimers, $C_8H_{10}Cl_2$, although neither was obtained quite pure. The lower-boiling dimer has been shown to be 3-*chloro*-1-α-*chlorovinyl*-Δ³-cyclo*hexene* (I). It yields on ozonolysis a crystalline *acid*, $C_8H_{11}O_4Cl$, m. p. 152—154°, which must be 3-α-*chlorovinyladipic acid* (II), since on ozonolysis it gives in theoretical yield butane-αβδ-tricarboxylic acid (III). The inertness of ethylenic linkages to the action of ozone has been previously recorded (Escott and Linstead, J., 1930, 914; Penfold, Ramage, and Simonsen, J., 1939, 1499).



On catalytic hydrogenation the chloro-acid gives 3-*ethyladipic acid* (IV), m. p. 47—48°. This acid appears to be new, and attempts to prepare it from β-acetyladipic acid failed, for this acid is not reduced by the Clemmensen method or by the action of sodium ethoxide on its semicarbazone or hydrazone. The liquid lactone, prepared by reduction of the keto-acid with sodium amalgam, also resists further reduction by hydriodic acid. Similar instances of the stability of keto-acids have been observed by Birch and Robinson (J., 1942, 485). The acid is not identical with α-ethyladipic acid, m. p. 49°, for which a simple method of preparation from ethyl 1-ethyl*cyclo*pentan-2-one-1-carboxylate is described. On catalytic hydrogenation 3-chloro-1-α-chlorovinyl-Δ³-*cyclo*hexene gives ethyl*cyclo*hexene.

Although the formation of this chloro*cyclo*hexene derivative was anticipated, since it is a simple adduct of the Diels–Alder type, yet that of the higher-boiling dimer, found to be 1 : 5-*dichloro*-Δ¹·⁵-cyclo*octadiene* (V), was unexpected, since there is no recorded case of cyclisation by head-to-tail union in this manner. The assignment of a *cyclo*octadiene structure to this dimer is based upon the following considerations. It contains two ethylene linkages, since it absorbs 4 molecules of hydrogen on catalytic hydrogenation to yield *cyclo*octane (VI). The identity of this hydrocarbon with that prepared by Willstätter *et al.* (*Ber.*, 1908, **41**, 1480; 1910, **43**, 1076) and by Zelinsky and Freimann (*ibid.*, 1930, **63**, 1480) was established by its oxidation to suberic acid by nitric acid.



The position of the two ethylenic linkages was proved by ozonolysis of the chloride to succinic acid, obtained in a 76·7% yield of that required for the formation of 2 mols. of the acid from one of the chloride. A further product of the ozonolysis was an aldehydo-acid, probably (VII), isolated as its 2 : 4-*dinitrophenylhydrazone*, $C_{14}H_{12}O_8N_4Cl$, m. p. 119°.

Experimental.

22 Kg. of the still residue remaining after the removal of monomeric chloroprene were fractionated under diminished pressure (3—4 mm.), and after removal of the xylene the following fractions were obtained: (1) low-boiling xylene mixture (94 g.), (2) b. p. 66—70° (450 g.), (3) b. p. 84—85° (320 g.), (4) b. p. 95—104° (75 g.). Fractions (2) and (3) were refractionated to yield 3-*chloro*-1-α-*chlorovinyl*-Δ³-cyclo*hexene*, b. p. 66—67°/4 mm., and 105°/20 mm., $d_{20°}^{20°}$ 1·1533—

1·168, $n_D^{24°}$ 1·51565, $[R_L]_D$ 46·4; calc., 45·74 (Found: C, 55·45; H, 5·75; Cl, 38·9. $C_8H_{10}Cl_2$ requires C, 54·25; H, 5·65; Cl, 40·1%), and 1 : 5-*dichloro*-Δ¹:⁵-cyclo*octadiene*, b. p. 84—85°/2 mm., 126°/18 mm., $d_{25°}^{25°}$ 1·174, $n_D^{25°}$ 1·5260, $[R_L]_D$ 46·28 (Found: C, 57·7; H, 6·3; Cl, 35·1%). On distillation both fractions decomposed slightly with evolution of hydrogen chloride, and this is reflected in the analytical data.

3-Chloro-1-α-chlorovinyl-Δ³-*cyclo*hexene is a colourless oil having a somewhat acrid odour and becoming brown on keeping. Its absorption spectrum has been examined by Dr. A. E. Gillam, of the University of Manchester, to whom we are indebted for the following report: "The absorption spectrum shows rising absorption at wave-lengths longer than 2240 A. The only selective absorption must therefore have its maximum below these wave-lengths. From the intensity of absorption at the limit reached (2240 A., ε = 1820) it can be safely inferred that a conjugated system of double bonds is absent." Attempts to eliminate hydrogen chloride by digestion with sodium methoxide or diethylaminoethanol were unsuccessful, although some dehalogenation did occur with the latter reagent. The polymer did not react with either maleic anhydride or α-naphthaquinone. In chloroform solution addition of bromine took place readily, a crystalline *tetrabromide* remaining on evaporation of the solvent. This separated from ligroin (b. p. 40—60°) in large, well-formed prisms, m. p. 146—147°, softening at 144° (Found: AgCl + AgBr, 207. $C_8H_{10}Cl_2Br_4$ requires AgCl + AgBr, 208%).

Hydrogenation of 3-*Chloro*-1-α-*chlorovinyl*-Δ³-cyclo*hexene*.—*Ethyl*cyclo*hexane*. On catalytic hydrogenation the absorption of hydrogen (4 mols.) was never complete, owing probably to poisoning of the catalyst by the hydrogen chloride formed. (It was later found that if this was absorbed by sodium acetate added initially, hydrogenation was complete.) In two micro-estimations using acetic acid as solvent and an Adams catalyst, the absorption was 2·35 c.c. and 4·14 c.c. in place of 3·17 and 4·83 c.c., respectively. In a macro-experiment with the polymer (13·34 g.), the hydrogen absorption was 6·26 l. (Calc. for $4H_2$: 6·76 l.). The hydrocarbon, ethyl*cyclo*hexane, isolated from the acetic acid solution, after neutralisation with sodium carbonate, by extraction with ether, had b. p. 130—131°/768 mm., $d_{25°}^{25°}$ 0·784, $n_D^{25°}$ 1·432 (Found: C, 85·45; H, 14·4. Calc. for C_8H_{16}: C, 85·7; H, 14·3%).

Ozonolysis of 3-*Chloro*-1-α-*chlorovinyl*-Δ³-cyclo*hexene*.—3-α-*Chlorovinyladipic acid*. The polymer (4·5 c.c.) in methyl acetate (50 c.c.) was ozonised at 0°, the issuing gases containing only traces of formaldehyde. After removal of the solvent under diminished pressure, the residual gum was mixed with water (10 c.c.) and gently warmed, the ozonide decomposing with considerable violence. The decomposition was completed by heating on the water-bath for 1 hour, the aqueous solution, which contained ionic chlorine, being evaporated. The residual oil (3·8 g.) crystallised, and after trituration with formic acid, the acid was collected and crystallised from this solvent. The *chloro-acid* separated in leaflets or bayonet-shaped needles, m. p. 152—154°, softening at 135° (Found: C, 46·3; H, 5·5; Cl, 16·9. $C_8H_{11}O_4Cl$ requires C, 46·5; H, 5·3; Cl, 17·1%). The *di*-p-*phenylphenacyl* ester crystallised from alcohol in small plates, m. p. 54—55° (Found: C, 72·3; H, 5·4. $C_{36}H_{31}O_6Cl$ requires C, 72·7; H, 5·2%).

The chloro-acid (1 g.) in methyl acetate (25 c.c.) was ozonised at 0°. The gummy ozonide, remaining after removal of the solvent, was decomposed with water (5 c.c.). Evaporation gave an oil (1 g.), which solidified. The acid crystallised from methyl acetate or acetone in rosettes of prisms, m. p. 121—122°, both alone and in admixture with butane-αβδ-tricarboxylic acid (Found: C, 44·1; H, 5·2. Calc. for $C_7H_{10}O_6$: C, 44·1; H, 5·3%).

Hydrogenation of 3-α-*Chlorovinyladipic Acid*.—3-*Ethyladipic acid*. In two micro-hydrogenations the acid absorbed 1·44 and 1·58 c.c. of hydrogen (Calc. for $2H_2$: 1·3 and 1·62 c.c., respectively). The acid (0·5 g.) was hydrogenated in alcohol by means of a palladium–norit catalyst; owing to an accident the volume of gas absorbed was not measured. After addition of alkali to the filtered solution, the alcohol was evaporated, and the acid isolated from the acidified solution by ether in the usual manner. 3-*Ethyladipic acid* crystallised from ether–ligroin (b. p. 40—60°) in needles, m. p. 47—49° (Found: C, 54·9; H, 7·9. $C_8H_{14}O_4$ requires C, 55·0; H, 8·0%). The *di*-p-*phenylphenacyl* ester crystallised from alcohol as a powder, seen under the microscope to consist of small prisms, m. p. 100—101° (Found: C, 76·4; H, 6·1. $C_{38}H_{34}O_6$ requires C, 76·1; H, 6·0%).

Ethyl 1-*ethyl*cyclo*pentan*-2-*one*-1-*carboxylate*. The *ester*, prepared by treating ethyl sodio*cyclo*pentan-2-one-1-carboxylate with ethyl iodide in benzene solution, had b. p. 115°/13 mm. (Found: C, 65·5; H, 8·6. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·7%). By digestion with alcohol containing sodium (1%) for 2 hours, *ethyl α-ethyladipate*, b. p. 133°/13 mm., was obtained (Found: C, 62·8; H, 9·5. $C_{12}H_{22}O_4$ requires C, 62·6; H, 9·5%). which on hydrolysis with hydrochloric acid gave α-ethyladipic acid, m. p. 47—49°. The *di*-p-*phenyphenacyl* ester crystallised from alcohol in balls of soft needles, m. p. 118—120°, depressed to 93° in admixture with the corresponding derivative of the β-ethyl acid (Found: C, 75·9: H, 6·1%).

1 : 5-*Dichloro*-Δ¹:⁵-cyclo*octadiene* is a colourless, mobile oil having a pleasant, terpene-like odour; it was somewhat unstable and darkened on keeping. The absorption spectrum as determined by Dr. A. E. Gillam shows only rising absorption at wave-lengths longer than 2240 A. There is an absorption band at 2650 A. (ε = 80). The intensity of the absorption at 2230 A. (ε = 1140) precludes the presence in the molecule of a conjugated system of double bonds. The presence of the band at 2650 A. is due probably to a small amount of a more strongly absorbing entity. The chloride did not react with either maleic anhydride or 1 : 4-naphthaquinone. In chloroform solution, bromine was rapidly absorbed but hydrogen bromide was vigorously evolved, and evaporation of the solvent left an oil.

Hydrogenation of the Chloride.—cyclo*Octane*. The chloride was hydrogenated in acetic acid solution by means of Adams's catalyst, but it was difficult to effect complete reduction. In three micro-hydrogenations the following results were obtained: 2·048, 6·722, and 7·017 mg. absorbed 0·71, 2·92, and 3·62 c.c., respectively, of hydrogen (Calc. for $4H_2$: 1·04, 3·4, 3·55 c.c.). On a larger scale, complete hydrogenation was only effected with considerable difficulty. The most satisfactory yield of hydrocarbon was obtained when an Adams catalyst was employed with acetic acid as the solvent with a hydrogen pressure of approx. 3 atm. After hydrogenation, the filtered acetic acid solution was neutralised with sodium carbonate, the hydrocarbon dissolved in ether, and the ether removed from the dried solution with the aid of a column. The *cyclo*octane prepared in this manner had b. p. 147—149°/743 mm., $d_{4°}^{25°}$ 0·831, $n_D^{25°}$ 1·4535 (Found: C, 85·5; H, 14·3. Calc. for C_8H_{16}: C, 85·7; H, 14·3%).

For oxidation to suberic acid, the hydrocarbon (1 g.) was mixed with nitric acid (*d* 1·42; 10 g.) and heated on the water-bath for 24 hours. On cooling, a crystalline solid separated, and was collected (0·4 g.); m. p. 133—135°, raised to 140—141° by crystallisation from water. The m. p. was unchanged in admixture with an authentic specimen of suberic acid (Found: C, 54·9; H, 7·9. Calc. for $C_8H_{14}O_4$: C, 55·1; H, 8·0%).

Ozonolysis of 1 : 5-*Dichloro*-Δ¹:⁵-cyclo*octadiene*.—The chloride (5 c.c.) in methyl acetate (50 c.c.) was ozonised at 0°, the issuing gases being passed through water, in which only a trace of formaldehyde could be detected at the conclusion of the oxidation. After removal of the solvent under diminished pressure, the ozonide was mixed with water (10 c.c.) and tended to decompose with explosive violence. The decomposition was completed by warming on the water-bath for 0·5 hour. On cooling the aqueous solution, which contained ionic chlorine, a crystalline solid (3·5 g.) was deposited, which was identified as succinic acid by m. p. 187°, both alone and in admixture, and by the preparation of the di-*p*-bromophenacyl ester, m. p. 214—215°, crystallising from acetic acid in leaflets. The aqueous mother-liquor, from which the succinic acid had been separated, was concentrated, yielding a further quantity (1·2 g.) of the same acid. The filtrate was made alkaline with sodium carbonate, and oxidised at 0° with potassium permanganate (1%). Isolation of the

organic acid from the filtered and concentrated alkaline solution by ether in the usual manner gave a further quantity of succinic acid (1·3 g.).

In one experiment the original aqueous filtrate from the succinic acid was mixed with aqueous 2 : 4-dinitrophenylhydrazine sulphate, a yellow 2 : 4-*dinitrophenylhydrazone* being deposited. This crystallised from alcohol in reddish-yellow needles, m. p. 119°, after softening at 115° (Found : C, 45·1; H, 4·3. $C_{14}H_{15}O_6N_4Cl$ requires C, 45·3; H, 4·0%), and was probably derived from the aldehydo-acid (VII).

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38. 5-(p-*Aminobenzenesulphonamido*)*thiazole.*

By M. H. M. ARNOLD and C. W. SCAIFE.

5-(p-*Aminobenzenesulphonamido*)*thiazole*, isomeric with sulphathiazole, is prepared from 5-amino-2-thioamidothiazole (I) by acylation, followed by removal of the $CS{\cdot}NH_2$ group. Although it has considerable bacteriostatic power, it is not pharmaceutically promising. The only derivatives of (I) that can be prepared without first protecting the amino-group are the nitrile and the *amide*.

WALLACH (*Ber.*, 1874, **7**, 902) obtained a compound, $C_4H_5N_3S_2$, which he called " chrysean," by passing hydrogen sulphide into a saturated aqueous solution of potassium cyanide. Hellsing (*Ber.*, 1899, **32**, 1497; 1900, **33**, 1774; 1903, **36**, 3546) prepared derivatives of it and showed that it was probably 5-amino-2-thioamidothiazole. We have confirmed the simple formula by molecular-weight determinations. Chrysean appeared to us to be of interest as a potentially cheap source of thiazole derivatives, and especially as a starting material for the synthesis of 5-(p-*aminobenzenesulphonamido*)*thiazole* for examination as a bactericide, " sulphathiazole " being 2-(*p*-aminobenzenesulphonamido)thiazole.

The earlier workers obtained chrysean in only 15—20% yield; we have been unable to increase this, but have improved the preparation by the replacement of potassium cyanide by sodium cyanide and by its acceleration with ammonia.

The chrysean molecule is fragile, and the 5-aminothiazole cannot be prepared by the nitrile, carboxylic acid, and decarboxylation route. Hellsing prepared 5-aminothiazole-2-nitrile from chrysean by treatment with lead or silver salts, but we have confirmed that attempts to hydrolyse this to the acid usually result in rupture of the ring, especially under alkaline conditions. Cautious acid hydrolysis has given 5-*aminothiazole*-2-*carboxylic acid* in poor yield. On the other hand, in neutral solution with excess of calcium carbonate the nitrile gives 5-*aminothiazole*-2-*amide* in very good yield. Hellsing showed that acylation of the amino-group permits normal degradation of the thioamide group, but that the products are all so resistant to hydrolysis that the acyl group cannot be removed. On the other hand, both 5-benzylideneaminothiazole-2-thioamide (Hellsing, *loc. cit.*) and 5-*benzylideneaminothiazole*-2-*nitrile* are too easily hydrolysed for this method of protecting the amino-group to be of any use.

The possibility of protecting the amino-group by diazotisation and formation of an azo-compound was then considered. Attempts to diazotise chrysean and the nitrile in the normal way gave highly coloured tars, which appeared to be formed by intermolecular condensation. 5-Aminothiazole-2-nitrile was diazotised by gradual addition of the solution to excess of hydrochloric acid and sodium nitrite at 0°. Chrysean is too sparingly soluble in water at 0° for this method to be successful, but diazotisation was achieved by adding its solution in pyridine to excess of nitrosyl chloride in benzene. This approach to the problem was not followed up.

It became clear that, since chrysean and its derivatives are only tractable when the amino-group is protected, appropriate acylation would have to precede attempts to remove the $-CS{\cdot}NH_2$ group. *p*-Nitrobenzenesulphonyl chloride gave 5-(p-*nitrobenzenesulphonamido*)*thiazole*-2-*thioamide*, which was converted into the 2-*nitrile*, and thence (or directly) into the 2-*carboxylic acid*, but this compound could not be decarboxylated satisfactorily. *p*-Acetamidobenzenesulphonyl chloride gave with chrysean 5-(p-*acetamidobenzenesulphonamido*)*thiazole*-2-*thioamide*, and with 5-aminothiazole-2-amide the corresponding 2-*amide*. 5-(*p*-Aminobenzenesulphonamido)thiazole was obtained from the 2-thioamide by converting this into the 2-nitrile (not isolated) and boiling the solution with sodium hydroxide; deacetylation, hydrolysis of the nitrile group, and decarboxylation then took place.

Dr. A. R. Martin of I.C. (Pharmaceuticals) Ltd., to whom our thanks are due, has examined 5-(*p*-acetamidobenzenesulphonamido)thiazole-2-thioamide and 5-(*p*-aminobenzenesulphonamido)thiazole for their bactericidal action, *in vitro* and *in vivo*, and has reported that against streptococcal infections in mice the latter substance, although active, has no advantage over established sulphonamide drugs, whereas the former substance is completely inactive.

EXPERIMENTAL.

5-*Aminothiazole*-2-*thioamide* (*Chrysean*).—Hydrogen sulphide (20—30 l./hr.) is passed into a saturated aqueous solution of sodium cyanide (200 g.) and a little ammonia; after a time plates appear. The chrysean is collected after 3—4 hours and recrystallised from hot water, forming yellow plates (25 g.), m. p. 204° (decomp.) (Found : C, 29·9; H, 3·1; N, 27·0; S, 39·7; *M*, cryoscopic in water, 155. Calc. : C, 30·2; H, 3·1; N, 26·4; S, 40·2%; *M*, 159). Acidific-

ation of the filtrate from the preparation of chrysean gives a flocculent reddish-brown precipitate in amount corresponding to 30—40% of the original cyanide (Found: C, 27·7; H, 2·7; N, 17·2; S, 46·3%). The substance, of high molecular weight, is soluble in alkali to give a deep brown solution; it is decomposed on heating with water to give hydrogen sulphide and a black alkali-soluble tar.

Attempts to increase the Yield of Chrysean:

Method.		Temp.	Yield of chrysean, %.	Rate of reaction.
1	H_2S into sat. aq. KCN (Wallach)	Room	15—20	—
2	H_2S into sat. aq. NaCN	,,	15—20	As (1)
3	H_2S into sat. aq. NaCN	0°	15—20	Much lower
4	H_2S into sat. aq. NaCN + NaOH	Room	15—20	Accelerated
5	H_2S into sat. aq. NaCN + dil. NH_3	,,	15—20	Much accelerated
6	H_2S into sat. aq. NaCN + dil. acid	,,	nil	—
7	Dil. AcOH added to theoretical amounts of NaCN + Na_2S	,,	nil	—
8	NaCN aq. added to NH_4Cl + Na_2S solution	,,	nil	—
9	NaCN aq. added to NH_4Cl + Na_2S solution sat. with H_2S	,,	nil	—
10	NaCN aq. added to NH_3 aq. sat. with H_2S	,,	nil	—
11	Liquid H_2S + solid HCN at 15 ats.	,,	nil	—
12	H_2S, HCN and trace of NaOH aq. at 15 ats.	,,	nil	—
13	H_2S + NaCN aq. at 15 ats.	,,	17—25 (product dark and difficult to purify)	—
14	H_2S into $(Ca(OH)_2$ + HCN) solution	,,	nil	—
15	H_2S, HCN, and trace NH_4OH at 15 ats.	,,	nil	—
16	$H{\cdot}CS{\cdot}NH_2$ + KCN solution	,,	15	—

High yields of chysean are invariably accompanied by large amounts of the by-product of high molecular weight.

5-Aminothiazole-2-nitrile (Hellsing's method, *loc. cit.*, slightly modified).—10 G. of chrysean were refluxed with 23·9 g. of lead acetate in 70 ml. of water for 3 hours, lead sulphide removed, and the filtrate evaporated to small volume, cooled in ice-water, and kept overnight. The product, recrystallised from water, formed fine yellow needles, m. p. 103° (Hellsing, m. p. 103°) (Found: C, 37·9; H, 2·9; N, 33·2; S, 25·8. Calc.: C, 38·4; H, 2·4; N, 33·6; S, 25·6%).

5-Aminothiazole-2-amide.—10 G. of chrysean were treated as above to give a solution of the crude nitrile; to the filtrate from lead sulphide was added precipitated calcium carbonate slightly in excess of that required to neutralise the acetic acid present, and the mixture refluxed for 2 hours. After filtration, the solution was evaporated cautiously to dryness, and the solid recrystallised from ether (alcohol easier for large amounts), affording in good yield small lemon-yellow crystals (not decolorised by charcoal) of *5-aminothiazole-2-amide*, decomp. 156° (Found: C, 33·8; H, 3·8; N, 29·6; S, 21·9. $C_4H_5ON_3S$ requires C, 33·5; H, 3·5; N, 29·4; S, 22·2%).

5-Aminothiazole-2-carboxylic Acid.—5-Aminothiazole-2-nitrile was refluxed with dilute hydrochloric acid, and a red flocculent precipitate obtained. Recrystallisation from alcohol gave a small yield of small colourless crystals of the *2-carboxylic acid*, decomp. 185° (Found: S, 22·0. $C_4H_4O_2N_2S$ requires S, 22·2%).

5-Benzylideneaminothiazole-2-nitrile.—10 G. of 5-aminothiazole-2-nitrile were dissolved in ethyl alcohol and refluxed with 8·5 g. of benzaldehyde. Small needles separated; these were removed, and the liquor concentrated to give a further crop of crystals. Recrystallisation from alcohol gave a good yield of small, light yellow needles of *5-benzylideneaminothiazole-2-nitrile*, m. p. 141° (Found: S, 14·9. $C_{11}H_7N_3S$ requires S, 15·0%).

5-(p-Nitrobenzenesulphonamido)thiazole-2-thioamide.—To a stirred suspension of 9 g. of chrysean in 30 ml. of pyridine cooled in ice-water, 11·2 g. of *p*-nitrobenzenesulphonyl chloride were added during 1 hour. The solution was kept at room temperature for 1 hour, diluted with 100 ml. of water, and acidified with dilute hydrochloric acid until just acid to Congo-red, the mixture being ice-cooled during acidification. After 12 hours the solid was collected and mixed with 200 ml. of water, and dilute aqueous ammonia added until the mixture was alkaline to thymol-blue. The solution was filtered, decolorised with charcoal, and acidified with dilute hydrochloric acid, and the precipitate of *5-(p-nitrobenzenesulphonamido)thiazole-2-thioamide* recrystallised from alcohol; m. p. 185° (decomp.) (Found: C, 34·0; H, 2·8; N, 15·7. $C_{10}H_8O_4N_4S_3$ requires C, 34·9; H, 2·3; N, 16·3%).

5-(p-Nitrobenzenesulphonamido)thiazole-2-nitrile.—7 G. of 5-aminothiazole-2-nitrile in 30 ml. of pyridine were treated with 11·2 g. of *p*-nitrobenzenesulphonyl chloride as in the preceding preparation. *5-(p-Nitrobenzenesulphonamido)thiazole-2-nitrile*, recrystallised from alcohol, had m. p. 148° (Found: C, 38·5; H, 2·0; N, 17·8; S, 20·6. $C_{10}H_6O_4N_4S_2$ requires C, 38·7; H, 1·9; N, 18·1; S, 20·6%).

5-(p-Acetamidobenzenesulphonamido)thiazole-2-thioamide, similarly prepared from 9 g. of chrysean in 30 ml. of pyridine and 11·6 g. of *p*-acetamidobenzenesulphonyl chloride and recrystallised from alcohol, had m. p. 237° (decomp.) (Found: C, 41·1; H, 3·4; N, 16·0; S, 26·7. $C_{12}H_{12}O_3N_4S_3$ requires C, 40·4; H, 3·4; N, 15·7; S, 26·9%).

(With Mr. J. Starr.) *5-(p-Acetamidobenzenesulphonamido)thiazole-2-amide*, prepared from 9·1 g. of 5-aminothiazole-2-amide, 34 ml. of pyridine, and 13·2 g. of *p*-acetamidobenzenesulphonyl chloride and recrystallised from water, had m. p. 253—255° (decomp.) (Found: C, 41·9; N, 16·2; S, 18·7. $C_{12}H_{12}O_4N_4S_2$ requires C, 42·4; N, 16·5; S, 18·8%).

5-(p-Aminobenzenesulphonamido)thiazole.—A solution of 21·36 g. of 5-(acetamidobenzenesulphonamido)thiazole-2-thioamide in 214 ml. of 10% aqueous sodium hydroxide was shaken with 16·03 g. of lead carbonate, filtered from lead sulphide, refluxed for 3 hours, and cooled. After filtration from a small amount of lead sulphide, it was acidified with 10% sodium bisulphate solution. The small yellow crystals obtained were recrystallised from boiling water, affording a moderately good yield of small needles or plates of *5-(p-aminobenzenesulphonamido)thiazole*, m. p. 185° (decomp.) (Found: C, 43·0; H, 3·5; N, 16·7; S, 24·9. $C_9H_9O_2N_3S_2$ requires C, 42·3; H, 3·5; N, 16·5; S, 25·1%).

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39. *The Union of Gaseous Oxygen with Methyl Oleate at 20° and 120°.*

By D. Atherton and T. P. Hilditch.

Oxygen was agitated with methyl oleate at 20° and 120° and the products obtained were partially separated by adsorption on silica gel. Portions of the separated products were oxidised in acetone solution with potassium permanganate, and the amount and nature of the mono- and di-carboxylic acid scission products examined.

The oxidised ester from the experiment at 20° yielded substantial proportions of suberic and octoic, as well as of azelaic and nonoic, acids, thus proving that to a large extent (although not necessarily exclusively) peroxidation had occurred at the $-CH_2-$ groups adjacent to the ethenoid bond (cf. Farmer *et al.*, *Trans. Faraday Soc.*, 1942, **38**, 134, 348, 356; J., 1943, 119).

The oxidised esters from the experiment at 120° gave much smaller yields of these mono- and di-carboxylic acids; the latter, moreover, contained only traces of suberic acid, and octoic acid could not be detected, nonoic and azelaic acids alone being obtained in quantity. At the higher temperature oxygen therefore appears to combine directly with the ethenoid bond, and in addition further changes of a more complex character probably take place, leading to oxidation at other points of the carbon chain.

Farmer and co-workers (J., 1943, 119) have recently shown that photochemical autoxidation of methyl oleate at 35° involves conversion of a $-CH_2-$ group adjacent to the ethenoid bond into a hydroperoxide $-CH(O{\cdot}OH){\cdot}CH{:}CH-$. Other investigators (*e.g.*, Morrell *et al.*, *J. Oil Col. Chem. Assoc.*, 1929, **12**, 183; 1936, **10**, 264, 359; *Trans. Faraday Soc.*, 1942, **38**, 262), studying the autoxidation of conjugated systems (elæostearic derivatives), have demonstrated that with these compounds a peroxide is produced at the double bond itself, which may undergo rearrangement into a ketol, $-CO{\cdot}CH(OH)-$. The explanation of the variant observations may be connected with the temperature at which the action of oxygen on the unsaturated fatty derivative takes place, or on the nature of the latter (monoethenoid, non-conjugated multi-ethenoid, or conjugated multi-ethenoid). It appeared that the method of disruptive oxidation by means of powdered permanganate in acetone solution (Armstrong and Hilditch, *J. Soc. Chem. Ind.*, 1925, **44** 43T) which has proved useful in determining the position of ethenoid linkings in unsaturated long-chain acids, might throw further light on the course of autoxidation of these compounds under different conditions. Whilst union of oxygen with the ethenoid bond itself would be expected to afford an oxidised product which would give the same scission products (azelaic and nonoic acids) as the unoxidised compound, the mechanism suggested by Farmer *et al.* should involve the appearance of suberic and octoic acids in addition, on further oxidation of an autoxidised oleic derivative.

We have examined the autoxidised products obtained from methyl oleate at 20° and 120° in the manner outlined above, and have found that the course of the action is very different according to the temperature employed. Other experiments on similar lines are in progress in which the products of autoxidation of methyl linoleate, linolenate and elæostearate will be similarly examined.

Autoxidation of Methyl Oleate by Oxygen at 20°.—Methyl oleate (containing a small proportion of methyl linoleate) was stirred with oxygen in bright daylight at room temperature (*ca.* 20°) over a prolonged period amounting in all to 34·5 days (*i.e.*, 24-hour periods). At the end of this time its peroxide value was 920 (calc. for complete conversion into peroxide, 3050) and its iodine value 72·7. This fall in iodine value is greater than that demanded by the exclusive formation of hydroperoxide, but only about half of that which would occur if the peroxide were wholly that produced by union of oxygen with the double bond. Moreover, as the following figures show, this relationship persisted throughout the autoxidation :

Time of exposure (days).	Peroxide value.	Peroxide,[1] %.	Iodine value.		
				Drop in I.V.	
			Observed.	Observed.	Calc.[2]
0	0	—	89·8	—	—
9·5	323	10·6	85·2	4·6	9·1
14	497	16·3	83·2	6·6	14·0
20·5	646	21·2	78·6	11·2	18·2
27	840	27·5	75·7	14·1	24·6
34·5	920	30·2	72·7	17·1	27·1

[1] Calculated from the theoretical full peroxide value of 3050.
[2] Calculated on the assumption that the peroxide is formed at the double bond, and its iodine value nil.

These figures therefore suggest that the autoxidation at 20° did not follow exclusively either of the supposed mechanisms, unless all the reduction in iodine value could be accounted for by secondary interaction of hydroperoxide with methyl oleate.

The final product was dissolved in light petroleum and separated into fractions by passage through a column of powdered silica gel, and subsequent development of the adsorbate with fresh light petroleum. About half of the ester passed through into the filtrates; this portion had I.V. 81 and a peroxide value of 170 (for details see Experimental, p. 107) and thus consisted very largely of unoxidised methyl oleate. The mean iodine and peroxide values calculated from those of the fractions separated by adsorption were 76·3 and 734, *i.e.*, respectively higher and lower than those (72·7 and 920) of the original oxidised ester. This is ascribed to some loss of oxygen and restoration of unsaturation during heating under reduced pressure (in order to remove the last traces of solvent), a feature previously noted by Hilditch and Lea (J., 1928, 1577). It may be observed that an increase of 3·6 units of iodine value is accompanied by a fall of 180 units in peroxide value, figures

which are consistent with loss of oxygen from an ethenoid peroxide and equally inconsistent with loss of oxygen from a hydroperoxide (in which case an increase of 3·6 in iodine value corresponds with a fall of about 1300 in peroxide value).

The material left on the silica gel (40% of the whole) was eluted with acetone in six portions, which had iodine values of 51—63 and peroxide values of 1200—1350. These were re-assembled into two fractions, representing the adsorbates on the upper and the lower part of the column, for oxidation in acetone with permanganate. The yields of mono- and di-carboxylic acids obtained in this way were as follows :

	Fraction oxidised, g.	Unoxidised residue, g.	Acidic products. Monobasic, g.	Dibasic, g.	Combined yield of acids on material oxidised, %.
Upper adsorbate	8·45	1·34	2·35	3·06	76
Lower „	8·95	1·50	3·21	3·14	85

In each case the dicarboxylic acids were found to consist of a mixture of suberic and azelaic acids. The approximate amounts isolated were 0·7 g. of suberic and 1·0 g. of azelaic acid from the upper adsorbate, and 0·8 g. of suberic and 1·6 g. of azelaic acid from the lower adsorbate.

The monocarboxylic acids from the two permanganate–acetone oxdiations were combined and fractionated; fractions were then obtained with equivalents (148·3 and 150·7) intermediate between those of octoic and nonoic acids (144 and 158).

These results confirm Farmer's view that autoxidation of methyl oleate at the ordinary temperature involves conversion of the methylene group at carbon atom 8 or 11 of the acyl chain into hydroperoxide. The 8-hydroperoxido-oleic ester furnishes suberic and nonoic acids on oxidative scission, azelaic and octoic acids resulting similarly from 11-hydroperoxido-oleic ester. Since there is no evidence at present regarding the relative proportions in which the 8- and 11-hydroperoxides may be formed, it is not possible to judge, from the comparative yields of the four acids, whether production of hydroperoxide is the sole mechanism operative under these conditions. As already mentioned, however, the observed alterations in iodine value during autoxidation at 20°, and during recovery of the eluted products (cf. above), were considerably greater than would have been the case if hydroperoxide formation had been exclusive, and we consider that the results indicate that, whilst the latter may well preponderate at 20°, an appreciable proportion of the autoxidation product must be formed by union of oxygen with ethenoid groups.

Autoxidation of Methyl Oleate by Oxygen at 120°.—After stirring in presence of a current of oxygen at 120° for 6 hours, the iodine value of the methyl oleate was reduced to 14·4, and the product was a viscous reddish-yellow oil, of which 22% (fraction A, iodine value 17·4) was insoluble in light petroleum. The portion soluble in light petroleum was adsorbed, as in the previous experiment, on a column of silica gel, the adsorbate being developed with light petroleum. The filtrates (30%, fraction C) had iodine values of 22—37, whilst the portions left adsorbed on the silica gel (48%, fraction B) had iodine values of 12—16. No unaltered oleate appeared to be present, but the products of autoxidation seemed to consist of three main groups differing somewhat in iodine value and, respectively, insoluble in light petroleum, soluble in the latter but unadsorbed by silica gel, and soluble in light petroleum but adsorbed from solution by silica gel. Each group was oxidised with permanganate, fractions A and B in acetone solution, and fraction C (which resisted oxidation in acetone) in glacial acetic acid solution. The yields of mono- and di-carboxylic acids obtained were as follows :

	Fraction oxidised, g.	Unoxidised residue, g.	Acidic products. Monobasic, g.	Dibasic, g.	Combined yield of acids on material oxidised, %.
A (insoluble in light petroleum)	9·1	1·2	1·53	1·97	44
B (adsorbed on silica gel)	20·0	3·4	1·36	3·90	32
C (filtrates from silica gel)	12·1	0·8	3(?)	3·18	55

The weights of acids recovered, expressed as a percentage of the materials oxidised, were very much lower than those in the preceding experiment, which in turn were somewhat lower than those normally obtained from a fresh, unoxidised specimen of methyl oleate (90—95%; cf. Armstrong and Hilditch, *loc. cit.*). It is inferred that a considerable proportion of the scission products must have been acids of low molecular weight, which owing to their volatility or high solubility in water escaped isolation by the procedure employed. This suggests that, during autoxidation at 120°, points in the acyl chain other than the unsaturated centre are attacked by oxygen subsequently to the initial action at or adjacent to the ethenoid group.

Examination of each group of dicarboxylic acids showed that they consisted for the most part of azelaic acid. Only small amounts of suberic acid were isolated, the weights of crude suberic acid obtained from the dibasic acids (1·97 g., 3·90 g., and 3·18 g.) from fractions A, B, and C being respectively 0·10, 0·32, and 0·13 g. The crude monocarboxylic acids from permanganate–acetone oxidations of A, B, and C were fractionally distilled, fractions with equivalents of 158·6 and 166·4 being obtained; no indication of the presence of octoic acid was detected in this case.

The results of autoxidation of methyl oleate at 120° thus point to almost complete absence of hydroperoxide at the 8th or 11th carbon atom of the acyl chain. The action which takes place at this temperature appears to proceed exclusively at the ethenoid group itself, and is probably followed by secondary action at other points in the acyl chain; it is extremely rapid in comparison with that of the formation of hydroperoxides.

Experimental.

The methyl oleate employed had been distilled under 0·1 mm. pressure through a fractionating column in order to eliminate minor amounts of palmitic or lower saturated esters. Its iodine value, 89·8, showed that it contained a small proportion (4·5%) of methyl linoleate.

The autoxidations were carried out in a 250 c.c. three-necked flask, fitted with mechanical stirrer (*ca.* 300 r.p.m.), thermometer, inlet and outlet tubes. A current of oxygen was passed through the ester throughout the experiments.

Autoxidation of Methyl Oleate at 20°.—The ester (55·4 g.) was stirred with oxygen during daylight for a total period of 828 hours (equivalent to 34·5 days). The alterations in peroxide and iodine value during this period have been illustrated on p. 105. The pale yellow liquid product (48·6 g.) was dissolved in light petroleum (250 c.c., b. p. 40—60°), filtered from slight turbidity, and passed down a 14″ column of activated dried silica gel. No clearly visible bands of colour were observed. The adsorbate was developed by passage of further light petroleum (450 c.c.), the filtrates being collected in three portions. The column was drained and cut into six portions, each of which was eluted with acetone. The peroxide and iodine values of the esters recovered from each portion, and from the filtrates, were as follows :

	Wt., g.	Peroxide value.	Iodine value.
Column, top ½ inch	0·51	1231	56·9
,, ½—2½ inches	1·96	1214	50·6
,, 2½—4½ ,,	2·48	1350	54·3
,, 4½—7¼ ,,	4·08	1016	56·7
,, 7¼—11 ,,	5·84	1278	60·9
,, bottom 3 inches	3·42	1270	63·4
Filtrate, third (200 c.c.)	3·36	432	79·1
,, second (200 c.c.)	21·64	170	81·4
,, first (250 c.c.)	1·83	nil	76·1

The upper four portions (9·03 g.) and the lower two portions (9·26 g.) of oxidised esters from the column were respectively combined, and each was further oxidised in acetone solution with powdered potassium permanganate.

Upper portions of adsorbate. The four mixed fractions (8·45 g.) were dissolved in acetone (85 c.c.), and the solution kept at the boiling point during gradual addition of powdered potassium permanganate (35 g.); the action proceeded smoothly. The solvent was removed, and the product reduced with bisulphite and taken up in ether. The ethereal solution was washed with potassium carbonate solution until all acidic products were removed, and incompletely oxidised ester (1·34 g.) was recovered from the ether. The aqueous carbonate washings were made strongly alkaline with caustic potash (5 g.) and evaporated on the steam-bath to a small volume, the semi-ester of the dicarboxylic acids formed during the oxidation being concurrently hydrolysed. The concentrated solution was made acid and distilled in steam until 2 l. of aqueous distillate were collected; on extraction with ether these yielded 2·35 g. of monocarboxylic acids. The residue from the steam distillation was thoroughly extracted with ether, which removed 3·06 g. of solid dicarboxylic acids.

The dicarboxylic acids were first crystallised from chloroform, which deposited crude suberic acid (0·68 g., m. p. 130—135°); after several crystallisations from ethyl acetate the acid melted at 138—141° (unchanged when mixed with authentic suberic acid, m. p. 140—142°). The acids left in solution in the chloroform were recovered and crystallised from ethyl acetate, impure azelaic acid (0·65 g., m. p. 94—99°, unchanged when mixed with pure azelaic acid, m. p. 104°) being deposited. The ethyl acetate mother-liquors still contained acids which, on crystallisation from water, gave further small quantities (0·34 g. in all) of crude azelaic acid.

Lower portions of adsorbate. The two mixed fractions (8·95 g.) were oxidised in acetone (90 c.c.) with permanganate (36 g.), and the product worked up as in the preceding case. The initial action with permanganate was much more vigorous than in the former case. The products obtained were incompletely oxidised ester (1·50 g.), monocarboxylic acids (3·21 g.), and dicarboxylic acids (3·14 g.).

The dicarboxylic acids, on crystallisation from chloroform at 20°, gave crude suberic acid (0·79 g., m. p. 130—135°), which after recrystallisation melted at 135—140° (138—140° when mixed with suberic acid, m. p. 140—142°). The chloroform mother-liquors were cooled at 0° and then deposited crude azelaic acid (1·13 g.), which on crystallisation from water gave a product, m. p. 92—100° (unchanged when mixed with pure azelaic acid). The acids left in solution in chloroform at 0° were recovered and crystallised from water, further quantities (0·46 g.) of crude azelaic acid being isolated.

The monocarboxylic acids from both portions of the oxidised adsorbates (2·35 g. and 3·21 g.) were combined and distilled at 15 mm. pressure through a long electrically-heated and packed fractionating column; two fractions (0·40 g. and 1·89 g.) were obtained with equivalents of 148·3 and 150·7 respectively (Calc. for $C_8H_{16}O_2$, 144; for $C_9H_{18}O_2$, 158). The acids (0·67 g.) recovered from a fraction which preceded these and which also contained small proportions of aldehydic or ketonic compounds had an equivalent of 121, corresponding with a mixture of octoic and hexoic acids; the latter probably resulted from oxidation of the small proportion of linoleate present in the original ester.

Autoxidation of Methyl Oleate at 120°.—The ester (39·7 g.) was maintained at 120° whilst it was stirred with oxygen. The fall in iodine value was very rapid compared with the previously-described experiment at 20° :

Time (hours)	0	0·5	1·5	2·5	3·5	4·5	6·0
Iodine value	89·8	84·9	63·4	39·8	27·7	19·5	14·4

The product (a reddish-yellow oil) was taken up in light petroleum (b. p. 40—60°, 150 c.c.); an insoluble portion then separated, which was extracted twice with further portions (75 c.c.) of the solvent. The light petroleum solutions were united and passed down a 14″ column of activated dried silica gel, the adsorbate being further developed by washing with three successive portions (200 c.c. each) of light petroleum. No clearly visible bands of colour appeared on the column of silica gel, which, after draining, was cut into five portions, each being then eluted with acetone. In all, the following fractions were thus obtained :

	Wt., g.	Iodine value.	Colour and consistency.
Insoluble in light petroleum	9·30	17·4	Dark, viscous.
Column top fifth	3·97	12·0	Light yellow, mobile.
,, second fifth	6·16	12·6	,, ,, ,,
,, third fifth	3·56	13·3	,, ,, ,,
,, fourth fifth	3·25	16·2	,, ,, ,,
,, bottom fifth	2·96	15·4	,, ,, ,,
Filtrate fourth (200 c.c.)	0·50	27·1	Almost colourless.
,, third (200 c.c.)	1·00	26·5	Very pale yellow.
,, second (200 c.c.)	8·43	22·0	Light red-yellow.
,, first (250 c.c.)	2·80	37·4	Red-yellow.

Permanganate–acetone oxidations were conducted on the portion insoluble in light petroleum, the combined extracts from the silica gel, and the combined material from the filtrate.

Material insoluble in light petroleum. This (9·1 g.) was dissolved in actone (200 c.c.) and oxidised with permanganate (100 g.). The action proceeded normally except that, as in some other instances during these studies, a certain amount of gel formation occurred transiently in the early stages of the action; this behaviour has not been observed in oxidations of pure unsaturated fatty esters. After working up the products as described earlier, there were obtained incompletely oxidised ester (1·19 g.), monocarboxylic (1·53 g.), and dicarboxylic (1·97 g.) acids. As in the other two oxidations about to be described, the yield of oxidation products recovered was much below that normally observed. The dicarboxylic acids were completely soluble in chloroform at 0°, and on crystallisation from water yielded successive crops which consisted substantially of azelaic acid (m. p. 94—98°). The final aqueous mother-liquors contained acids, from an ethyl acetate solution of which 0·1 g. of very impure suberic acid (m. p. 120—129°, mixed m. p. with suberic acid, 125—130°) was isolated.

Material adsorbed by the silica gel. This (20·0 g.) was dissolved in acetone (250 c.c.) and oxidised with permanganate (125 g.). The products obtained were incompletely oxidised ester (3·39 g.), monocarboxylic (1·36 g.) and dicarboxylic (3.90 g.) acids. The latter deposited on prolonged standing in chloroform at 20° a small amount (0·19 g.) of crystals, m. p. 122—127°, which on recrystallisation from ethyl acetate melted at 129—130° (mixed m. p. with 9 : 10-dihydroxystearic acid, 130°). The 9 : 10-dihydroxystearic acid of m. p. 130° was not observed in any of the other oxidations carried out during this work. The remaining acids present proved to be almost entirely azelaic acid, with the exception of a small amount (0·32 g.) of very impure suberic acid, m. p. 126—138° (mixed m. p. with suberic acid, 129—136°), which was obtained when the acids from aqueous mother-liquors were dissolved in ethyl acetate and kept at 0° for several days.

Material in the light petroleum filtrates. This (12·1 g.) was dissolved in acetone (240 c.c.) and oxidised with permanganate (120 g.). The oxidation was unexpectedly difficult and there were obtained incompletely oxidised ester (5·36 g.), monocarboxylic (2·23 g.) and dicarboxylic (1·60 g.) acids. The latter consisted almost wholly of azelaic acid, but a very small amount (0·05 g.) of impure suberic acid was eventually isolated (m. p. 125—130°, unchanged when mixed with suberic acid).

The incompletely oxidised ester (5·36 g.) resisted further attack by permanganate in acetone solution; on solution in glacial acetic acid (60 c.c.) and gradual addition of permanganate (45 g.) no action took place in the cold but on gradual warming a very vigorous action set in which subsided when the mixture was cooled. Subsequently the action was maintained smoothly on the steam-bath for 2 hours; then a further, almost explosive, action set in. The products finally obtained were incompletely oxidised residue (0·79 g.), monocarboxylic acids (5·81 g., mainly acetic which had escaped complete removal) and dicarboxylic acids (1·58 g.) from which a further 0·08 g. of impure suberic acid (m. p. 124—133°, mixed m. p. 126—136°) was eventually isolated, the remainder being azelaic acid.

The monocarboxylic acids recovered from the three preceding permanganate–acetone oxidations (1·53, 1·36 and 2·23 g.) were united and fractionally distilled at 15 mm. pressure. Two fractions (0·74 g. and 1·67 g.) were obtained which had equivalents of 158·6 and 166·4 respectively, so that no evidence was forthcoming of the presence of any octoic acid.

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40. Delphinium *Alkaloids. Part II. Ajacine.*

By JOHN A. GOODSON.

Ajacine yields as products of hydrolysis lycoctonine and acetic and anthranilic acids and hence has the formula $C_{34}H_{46}O_9N_2,2H_2O$.

AJACINE was first isolated from the seeds of *Delphinium ajacis* by Keller and Völker (*Arch. Pharm.*, **1913**, **251**, 209), who assigned to it the formula $C_{15}H_{21}O_4N,H_2O$. Recently, Hunter (*Pharm. J.*, **1943**, **150**, 82) proposed the formula $C_{32}H_{44}O_8N_2,2H_2O$.

As it was thought that ajacine might be closely related to lycaconitine from *Aconitum lycoctonum*, which Schulze and Bierling (*Arch. Pharm.*, **1913**, **251**, 8) showed to be succinylanthranoyl-lycoctonine, and to methyl-lycaconitine from *D. elatum*, which Goodson (J., 1943, 139) found to be methylsuccinylanthranoyl-lycoctonine, it has been submitted to hydrolysis. Alkaline hydrolysis gives acetylanthranilic acid and lycoctonine according to the equation $C_{34}H_{46}O_9N_2 + H_2O = C_{25}H_{39}O_7N + C_9H_9O_3N$ and acid hydrolysis yields acetic acid and anthranoyl-lycoctonine: $C_{34}H_{46}O_9N_2 + H_2O = CH_3{\cdot}CO_2H + C_{32}H_{44}O_8N_2$. From this it follows that ajacine is acetylanthranoyl-lycoctonine and has the empirical formula $C_{34}H_{46}O_9N_2,2H_2O$.

EXPERIMENTAL.

The m. p.'s are corrected.

Ajacine crystallised from the concentrated ethereal solution of the alkaloids liberated by sodium bicarbonate from the solution of the total alkaloids of *D. ajacis* seeds in dilute hydrochloric acid. The *base*, purified by crystallisation from 70% alcohol, gave needles with two molecules of water, m. p. 154° (sintering at 150°), $[\alpha]_D^{22°}$ + 49·5° (*c* = 2 in dry alcohol), $[\alpha]_D^{22°}$ + 30·8° (*c* = 2 in N/5-hydrochloric acid) (Found: C, 61·5; H, 7·8; N, 4·5; OMe, 17·5; NMe, 4·0; loss at 105° in a vacuum, 5·4. $C_{34}H_{46}O_9N_2,2H_2O$ requires C, 61·6; H, 7·6; N, 4·2; 4OMe, 18·7; NMe, 4·4; $2H_2O$, 5·4%).

Alkaline Hydrolysis of Ajacine.—Ajacine (5 g.) was dissolved in alcohol (125 c.c.) and heated on the water-bath with 17 c.c. of N-sodium hydroxide until most of the alcohol had evaporated. On addition of water (125 c.c.), 2·54 g. of crude crystalline lycoctonine separated. A further 0·71 g. was extracted from the filtrate by chloroform. Crude crystalline acetylanthranilic acid (0·71 g.) separated on the addition of dilute sulphuric acid; a further 0·69 g. was obtained by extraction of the filtrate with chloroform. The lycoctonine, purified by recrystallisation from 70% alcohol, had $[\alpha]_D^{18°}$ + 53·0°, m. p. 141°, not depressed by lycoctonine obtained from the hydrolysis of methyl-lycaconitine from the seeds of *D. elatum* (Goodson, J., 1943, 141) (Found: equiv., by titration with N/10-sulphuric acid with methyl-red as indicator, 485. Calc. for $C_{25}H_{39}O_7N,H_2O$: equiv., 483).

The acetylanthranilic acid, recrystallised from boiling water, had m. p. 185°, not depressed by authentic acetylan-

thranilic acid (Found : C, 60·6; H, 5·2; N, 7·9; equiv., by titration with N/5-sodium hydroxide with phenolphthalein as indicator, 179·5. Calc. for $C_9H_9O_2N$: C, 60·3; H, 5·1; N, 7·8%; equiv., 179·1). Hydrolysis with dilute hydrochloric acid gave acetic and anthranilic acids.

Acid Hydrolysis of Ajacine.—Ajacine (5 g.) was dissolved in 50 c.c. of 10% hydrochloric acid and kept in a closed vessel for 14 days. On addition of excess of saturated solution of sodium carbonate, 4·7 g. of crude anthranoyl-lycoctonine were precipitated. The filtrate from the anthranoyl-lycoctonine was acidified with dilute hydrochloric acid and extracted with chloroform, which only removed a portion of the acetic acid produced. This was identified by conversion into the silver salt (Found : Ag, 64·3. Calc. : Ag, 64·6%). A further quantity of acetic acid was separated from the solution after extraction with chloroform as silver salt.

The anthranoyl-lycoctonine, purified by recrystallisation from 70% alcohol, had $[\alpha]_D^{18°}$ + 31·0° (c = 2 in N/5-hydrochloric acid), m. p. 172°, not depressed by anthranoyl-lycoctonine obtained by hydrolysis of methyl-lycaconitine from *D. elatum*. Its solution had a beautiful blue-violet fluorescence. On alkaline hydrolysis it gave anthranilic acid and lycoctonine.

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41. *A New Method of Nuclear Methylation of Aromatic Amines.*

By (MISS) M. G. BARCLAY, A. BURAWOY, and G. H. THOMSON.

A method of nuclear methylation of aromatic amines is described consisting in the heating to temperatures above 300° (*e.g.*, dry distillation) of the so-called anhydro-4-aminobenzyl alcohols (I or II). It is assumed that the reaction starts with the formation of radicals (III), which subsequently undergo disproportionation with formation of nuclear methylated amines (cf. IV) and unidentified oxidised resinous substances. Addition of an alkaline reagent is essential to obtain good yields. It prevents the condensation of anhydro-4-aminobenzyl alcohols to substances containing methylene linkages between several aromatic groups, which under such conditions decompose mainly with formation of the original amines.

IN an attempt to obtain *p*-toluidine by a method which did not involve toluene as starting material, the possibility of nuclear methylation of aniline and other aromatic amines was examined. The Hofmann reaction, consisting in the treatment of an aromatic amine with methyl alcohol and acid at high temperatures under pressure, fulfils this purpose, but it possesses certain disadvantages, *e.g.*, the necessity of working under high pressure, and in the case of the preparation of only partially nuclear methylated amines, such as *p*-toluidine, the formation of several products.

Aromatic primary and secondary amines with a free *p*-position react in presence of mineral acids with formaldehyde, forming anhydro-4-aminoaryl alcohols (Kalle and Co., B.P. 1895, 1963). These are polymers and should possess a ring or long-chain structure consisting of two or more molecules (I or II). In the latter case the free valencies of the terminal atoms would be saturated by the addition of a water or an aniline molecule. The same substances can also be obtained by other methods, *e.g.*, dehydration of 4-amino-aryl alcohols by heat or by a treatment with acids. We have now attempted to convert these substances into the corresponding

(I.) $[RN(H)—C_6H_4—CH_2]_n$ with $H_2C—C_6H_4—NR$; $RN(H)—[C_6H_4—CH_2—NR]_n—C_6H_4—CH_2$ (II.)

nuclear methylated aromatic amines. 4-Aminobenzyl alcohol and its anhydrides yield *p*-toluidine when reduced by zinc and mineral acid (D.R.P. 83,544), but the yields are unsatisfactory.

Hydrazobenzene when heated to high temperatures decomposes with formation of aniline and azobenzene (Hofmann, *Proc. Roy. Soc.*, 1863, **12**, 576), and it is likely that this reaction starts with the cleavage of the NH–NH linkage, forming free radicals Ar·NH·, which become stabilised by disproportionation involving undissociated hydrazobenzene :

$$NHPh·NHPh \longrightarrow 2NHPh·$$

$$2NHPh· + NHPh·NHPh \longrightarrow 2NH_2Ph + NPh{:}NPh$$

Hydrocarbons possessing aliphatic C–C linkages also decompose at high temperatures, starting with a cleavage of such a link and the formation of radicals, which become stabilised by disproportionation with other undissociated hydrocarbons, thus forming saturated hydrocarbons of smaller carbon content in addition to unsaturated hydrocarbons (cf. Rice and Rice, " The Aliphatic Free Radicals," Baltimore, 1935, pp. 91, 142). The stabilisation of free radicals by disproportionation appears to be a general phenomenon, probably first observed in the formation of triphenylmethane by heating of hexaphenylethane (Gomberg and Cone, *Ber.*, 1904, **37**, 2037; cf., *e.g.*, Marvel *et al.*, *J. Amer. Chem. Soc.*, 1939, **61**, 2769, 2771; Treckel and Selwood, *ibid.*, 1941, **63**, 3397) :

$$CH_2R·CH_2R \longrightarrow 2CH_2R·$$

$$2CH_2R· + CH_2R·CH_2R \longrightarrow 2CH_3R + CHR{:}CHR$$

We considered that, since the polymerised anhydro-4-aminobenzyl alcohols (I or II) contain CH_2–NH linkages which are intermediate between NH–NH and CH_2–CH_2 linkages, they might behave similarly, and form when heated to high temperatures in the first place radicals of the type (III; n = 0, 1, 2. . . .), which in turn would undergo disproportionation with formation of *p*-toluidine (IV; n = 0) or substances (IV; n = 1, 2 . . .) from which *p*-toluidine could be easily obtained during the heating.

(III.) $·NH—[C_6H_4·CH_2·NH]_n—C_6H_4·CH_2·$ $\longrightarrow$ $NH_2—[C_6H_4·CH_2·NH]_n—C_6H_4·CH_3$ (IV.)

$\longrightarrow$ $·NH—[C_6H_4·CH_2·NH]_{n-1}—C_6H_4·CH_2· + NH_2·C_6H_4·CH_3$

Indeed, anhydro-4-aminobenzyl alcohol, when heated to a high temperature under pressure or, more conveniently, when dry distilled, decomposes with formation of a mixture of almost equal parts of aniline and *p*-toluidine; in addition, small amounts of *N*-methyl-*p*-toluidine, high-boiling amines, and volatile amines (especially ammonia) are formed. The yield of the aniline–*p*-toluidine mixture is, however, less than 25%.

The formation of aniline from anhydro-4-aminobenzyl alcohol might be unexpected, and might lead to doubts about the structure of this substance prepared from aniline, mineral acid, and formaldehyde. However, 4-aminobenzyl alcohol, prepared by reduction of 4-nitrobenzyl alcohol, and the anhydro-4-aminobenzyl alcohol obtained from it, the structures of which are beyond doubt, behave in the same way.

Following up certain considerations to be discussed below, we have found that heating (dry distillation) of anhydro-4-aminobenzyl alcohol in an alkaline medium yields 35—40% of *p*-toluidine, accompanied by only negligible amounts of by-products. The improvement can be obtained in presence of alkaline substances such as sodium acetate, sodium bicarbonate, sodium borate, but the use of sodium carbonate or calcium hydroxide is preferable. Neutral diluents such as fuller's earth, kieselguhr, or sand have little or no effect on the yield and quality of the amines formed.

Anhydro-4-aminobenzyl alcohol obtained by dehydration of 4-aminobenzyl alcohol, and this alcohol itself give the same result. Other substances, which at the temperature required in these experiments decompose with formation of anhydro-4-aminobenzyl alcohol, and, consequently, behave similarly, are 4-aminobenzylaniline and similar derivatives.

Anhydro-4-aminobenzyl alcohol was prepared under different conditions, *i.e.*, with variation in the amount of formaldehyde or acid and in the temperature. The best results were obtained by first condensing 1 mol. of aniline hydrochloride with 1·2—1·5 mols. of formaldehyde below 20°. If this temperature or the acid concentration is increased, the anhydro-4-aminobenzyl alcohol is accompanied by increasing amounts of resins. Such products are also formed when anhydroaminobenzyl alcohol, obtained by dehydration of 4-aminobenzyl alcohol or by condensation of aniline, formaldehyde, and mineral acid below 20°, is treated with mineral acid on the water-bath. In this case, formaldehyde is split off, indicating the formation of CH_2 linkages between different aromatic groups completely analogous to those existing in phenol–formaldehyde resins.

Aromatic amines connected by methylene linkages, when heated above 400°, decompose with formation of aniline or its derivatives. The simplest representative, 4 : 4′-diaminodiphenylmethane (heated under pressure, since its b. p. lies below the decomposition temperature), yields a small amount of aniline and *p*-toluidine. Similarly, when the more complicated resinous methylene derivatives obtained from anhydro-4-aminobenzyl alcohol are heated above 400°, they decompose with formation of a negligible amount of *p*-toluidine and a small yield of aniline.

The formation and subsequent decomposition of such resinous products, when anhydro-4-aminobenzyl alcohol is heated in absence of alkaline substances to the high temperature required, explains the formation of aniline and a reduced total yield of amines. The function of these alkalis is to prevent formation of such products detrimental to the yield of *p*-toluidine. This is confirmed by the fact that distillation in the presence of alkalis of the above-mentioned condensation products, *e.g.*, obtained by treatment of anhydro-4-aminobenzyl alcohol with mineral acids at water-bath temperature, does not give the improved yield of *p*-toluidine.

This convenient and economical method of nuclear methylation can be applied to other aromatic amines with a free *p*-position, and in many cases is much superior to the existing methods. An alkaline medium is always required to give satisfactory yields (20—40%) of the desired methylated amines, for in its absence a mixture of the methylated aromatic amine with the original amine in a smaller total yield is obtained. In addition, varying amounts of by-products similar to those obtained in the case of anhydro-4-aminobenzyl alcohol, especially higher-boiling amines of the 4 : 4′-diaminodiphenylmethane type, are obtained. Typical examples are given later, but it should be realised that the amount of methylated amines may vary with the type and amount of the added alkaline substances.

Anhydro-4-amino-3-methylbenzyl alcohol (from *o*-toluidine) gives in presence of calcium hydroxide a good yield of *m*-4-xylidine in addition to some 4 : 4′-diamino-3 : 3′-dimethyldiphenylmethane, and the 2-methyl analogue (from *m*-toluidine) decomposes similarly with formation of *o*-4-xylidine. Anhydro-4-amino-2 : 5-dimethylbenzyl alcohol (from *p*-xylidine) yields in addition to ψ-cumidine some 4 : 4′-diamino-2 : 2′ : 5 : 5′-tetramethyldiphenylmethane. This method also allows the preparation of the hitherto unknown *4-amino-1 : 2 : 3-trimethylbenzene* (m. p. 24°) from anhydro-4-amino-2 : 3-dimethylbenzyl alcohol (from *o*-3-xylidine), the Hofmann reaction apparently leading to the formation of 1-amino-2 : 5 : 6-trimethylbenzene (Noelting and Forel, *Ber.*, 1885, **18**, 2680). Anhydro-4-amino-3-methoxybenzyl alcohol (from *o*-anisidine) gives only a moderate yield of 4-amino-3-methoxytoluene, whereas anhydro-4-amino-1-hydroxymethylnaphthalene (from α-naphthylamine) yields a mixture of similar amounts of α-naphthylamine and 4-methyl-1-naphthylamine, which can be separated by means of their picrates.

This reaction can be extended to the anhydro-4-aminoaryl alcohols derived from secondary amines. Dry distillation of anhydro-4-monomethylaminobenzyl alcohol (from monomethylaniline) in presence of calcium hydroxide yields *N*-methyl-*p*-toluidine and some *p*-toluidine. It appears that the methyl group attached to the nitrogen atom is liable to split off at the high temperature of the reaction, *viz.*, > 300° and generally 400—500°.

The fate of the oxidised part of the starting material, which serves as the source of hydrogen for the disproportionation, has not been investigated, for the resins produced are intractable.

Experimental.

Destructive Distillation of 4-Aminobenzyl Alcohol.—(i) 4-Aminobenzyl alcohol (37 g.; Fischer and Fischer, *Ber.*, 1895, **28**, 880) is heated under reflux on an air-bath for 30 mins., and then dry distilled. Fractions: < 200°, 3 g. (m. p. 15°); 200—210°, 5 g. (m. p. 10°); > 210°, 2 g. (oil). All fractions are mixtures of aniline and *p*-toluidine, identified in the usual manner. The approximate proportions may be indicated by the m. p.'s, if the small amounts of by-products are neglected: a mixture of equal parts of aniline and *p*-toluidine (m. p. 44°) melts at 14°. (ii) 4-Aminobenzyl alcohol (75 g.) and anhydrous sodium carbonate (75 g.) are thoroughly mixed, heated under reflux, and dry distilled as above; yield, 42 g. Fractions: 195—200°, 10 g. (m. p. 15°); 200—205°, 17 g. (m. p. 34°). These fractions contain only a small amount of aniline and consist mainly of *p*-toluidine. A small amount of a high-boiling viscous oil is also obtained. (iii) 4-Aminobenzyl alcohol (0·953 g. or 0·743 g.) is slowly heated with 5% sulphuric acid. Water containing formaldehyde (0·045 g. or 0·036 g.) is collected.

Anhydro-4-aminobenzyl Alcohol.—Preparation. Aniline hydrochloride (130 g., 1 mol.) is dissolved in water (600 g.) and a 37·5% aqueous formaldehyde solution (120 c.c., 1·5 mols.) added, the mixture being stirred and cooled. After 30 mins., water (720 c.c.) is added to the dark red, gelatinous product, and the mixture made alkaline with sodium carbonate. The colourless precipitate is filtered off and washed until free from alkali.

Dry distillation. (i) Anhydro-4-aminobenzyl alcohol (500 g.) yields 140 g. of a mixture of oil and solid. Fractions: 193—195°, 22 g. (m. p. 17°); 195—200°, 50 g. (m. p. 19°); 200—205°, 24 g. (m. p. 19°); 205—210°, 11 g. (m. p. 17°); 250—400°, 24 g. (thick oil). The lower-boiling fractions consist of aniline and *p*-toluidine, and contain small amounts of *N*-methyl-*p*-toluidine, identified by its nitroso-derivative. During the distillation, volatile amines, especially ammonia, are also formed. (ii) Anhydro-4-aminobenzyl alcohol (500 g.) is mixed with anhydrous sodium carbonate (500 g.) and dry distilled. Yield, 250 g. of a semi-solid mixture. Fractions: < 195°, 20 g. (m. p. 19°); 195—200°, 167 g. (m. p. 35°); 200—205°, 15 g. (m. p. 29°); 205—210°, 8 g. (m. p. 20°); 210—270°, 15 g. (thick oil); residue, 14 g. The fractions, b. p. 195—205°, consist almost entirely of *p*-toluidine; the first fraction contains also an appreciable amount of aniline, and those above 205° some *N*-methyl-*p*-toluidine. (iii) The alcohol (500 g.) is mixed with calcium hydroxide (500 g.) and dry distilled. Yield, 283 g. of a semi-solid mixture. Fractions: 198—200°, 138 g. (m. p. 25°); 200—205°, 52 g. (m. p. 37°); 205—220°, 20 g. (m. p. 28°); high-boiling residue, 60 g. (thick oil). The first fraction contains in addition to *p*-toluidine a small amount of aniline, the third some *N*-methyl-*p*-toluidine. (iv) Dry distillation in presence of zinc, copper, iron, kieselguhr, sand, fuller's earth and similar neutral substances, or in presence of acids, does not give better yields of *p*-toluidine than method (i). (v) Anhydro-4-aminobenzyl alcohol (100 g.) is heated with concentrated hydrochloric acid (100 c.c.) and water (500 c.c.) at 70° for 3 hours. The mixture is then neutralised, and the precipitate filtered off, washed, and dried. A portion of this substance (84 g.) is mixed with sodium carbonate (83 g.) and dry distilled. Yield, 31 g. Fractions: < 180°, 3 g. (oil); 180—200°, 5 g. (m. p. 16°); 200—204°, 6 g. (m. p. 12°); high-boiling fraction, 16 g. (vi) Quantities as in (v) are heated at 100° for 1 hour, and the product treated as in (v). A portion (85 g.) and sodium carbonate (85 g.) are dry distilled. Yield, 38 g. Fractions: < 180°, 3 g. (oil); 180—195°, 6 g. (m. p. 10°); 195—202°, 10 g. (m. p. 13°); high-boiling fraction, 18 g. (vii) Aniline hydrochloride (130 g.), water (600 c.c.), and 37·5% aqueous formaldehyde solution (80 c.c.) are heated at 70° for 30 mins.; the mixture is made alkaline, and the precipitate filtered off, washed, and dried. A portion (138 g.) and calcium hydroxide (138 g.) are distilled. Yield, 43 g. Fractions: < 190°, 8 g. (oil); 190—198°, 9 g. (m. p. 16°); 198—204°, 12 g. (m. p. 26°); high-boiling fraction, 9 g.

Dry Distillation of 4-Aminobenzylaniline.—4-Aminobenzylaniline (50 g.; Paal and Sprenger, *Ber.*, 1897, **30**, 70) is mixed with calcium hydroxide (50 g.) and dry distilled. Yield 38 g. (oil). Fractions: < 192°, 18·5 g. (m. p. 4°); 192—205°, 9 g. (m. p. 8°); *i.e.*, a mixture of aniline and *p*-toluidine.

Decomposition of 4 : 4′-Diaminodiphenylmethane.—This substance (25 g.) is heated under pressure at 400° for 18 hours. The product is steam-distilled, and the distillate extracted with ether and redistilled. Yield, 4 g. of a mixture consisting of aniline and *p*-toluidine.

Anhydro-4-amino-3-methylbenzyl Alcohol.—Preparation. *o*-Toluidine hydrochloride (143·5 g., 1 mol.) is dissolved in water (1 l.) and 37·5% aqueous formaldehyde (120 c.c., 1·5 mol.) added, the mixture being stirred and cooled. After 30 mins., the mixture is made alkaline with sodium hydroxide, and the white precipitate filtered off, washed, and dried.

Dry distillation. (i) Anhydro-4-amino-3-methylbenzyl alcohol (440 g.) afforded 155 g. of an oil. Fractions: 200—205°, 20 g.; 205—210°, 76 g.; 210—220°, 38 g.; 220—245°, 6 g. The first three fractions are a mixture of *o*-toluidine (b. p. 197°) and *m*-4-xylidine (b. p. 212°; benzoyl derivative, m. p. and mixed m. p. 192°). (ii) The alcohol obtained from *o*-toluidine (436 g.) is mixed with calcium hydroxide (500 g.) and dry distilled. Yield, 270 g. (oil). Fractions: < 211°, 34 g.; 211—214°, 134 g.; high-boiling fraction, 87 g. The fractions below 215° consist of *m*-4-xylidine and a very small amount of *o*-toluidine; from the high-boiling fraction, 4 : 4′-diamino-3 : 3′-dimethyldiphenylmethane (72 g.) is isolated; m. p. and mixed m. p. 153°.

Anhydro-4-amino-2-methylbenzyl Alcohol.—m-Toluidine hydrochloride (430·5 g., 3 mols.) is dissolved in water (3 l.), and 37·5% aqueous formaldehyde solution (360 c.c., 4·5 mols.) added. After being stirred at 12° for 30 mins., the mixture is made alkaline. The precipitate is filtered off, washed, dried, thoroughly mixed with calcium hydroxide (450 g.), and dry distilled. Yield, 180 g. (oil). Fractions: < 220°, 13 g.; 220—229°, 110 g.; high-boiling product, 44 g. The fractions below 229° consist almost entirely of *o*-4-xylidine (m. p. 48°, after one recrystallisation from light petroleum; pure *o*-4-xylidine, b. p. 224°; m. p. 48°).

Dry Distillation of Anhydro-4-amino-2 : 5-dimethylbenzyl Alcohol.—(i) The alcohol, prepared from *p*-xylidine (1 mol.), hydrochloric acid (1 mol.), and 37·5% aqueous formaldehyde solution (1·1—1·5 mols.), affords 73 g. of distillate. Fractions: 212—225°, 35 g.; 225—250°, 19 g.; 250—270°, 11 g. The first two fractions contain about equal amounts of *p*-xylidine (b. p. 215°) and ψ-cumidine (b. p. 234°; m. p. 68°). (ii) The alcohol (obtained from *p*-xylidine, 385 g.) is thoroughly mixed with calcium hydroxide (400 g.) and dry distilled. Yield, 203 g. of a semi-solid mixture. Fractions: < 230°, 12 g.; 230—240°, 76 g.; 240—250°, 15 g.; high-boiling fraction, 61 g. The first fraction contains *p*-xylidine and mainly ψ-cumidine, the second and third almost pure ψ-cumidine [m. p. 66°, after one recrystallisation from light petroleum (b. p. 60—80°)], and the last consists mostly of 4 : 4′-diamino-2 : 5 : 2′ : 5′-tetramethyldiphenylmethane (after one crystallisation from light petroleum, m. p. and mixed m. p. with an authentic specimen, 139°).

Dry Distillation of Anhydro-4-amino-2 : 3-dimethylbenzyl Alcohol.—This substance is obtained as usual from *o*-3-xylidine hydrochloride (315 g.) and 37·5% aqueous formaldehyde solution (250 c.c.) as a white powder. It is mixed with calcium hydroxide (350 g.) and dry distilled. Yield, 127 g. (oil). Fractions: < 230°, 12 g.; 230—240°, 45 g.; 240—250°, 36 g.; high-boiling fraction, 18 g. The lower-boiling fractions contain a little *o*-3-xylidine (b. p. 222°), but mostly 4-*amino*-1 : 2 : 3-*trimethylbenzene* (b. p. 238—240°; m. p. 24°) (Found: N, 10·6. $C_9H_{13}N$ requires N, 10·4%); *acetyl* derivative, m. p. 140° (Found: N, 8·2. $C_{11}H_{13}ON$ requires N, 7·9%).

Dry Distillation of Anhydro-4-amino-3-methoxybenzyl Alcohol.—A sample obtained from *o*-anisidine (123 g.) is mixed with calcium hydroxide (150 g.) and dry distilled. Fractions: < 225°, 5 g.; 225—235°, 17 g., mostly 3-methoxy-*p*-toluidine (b. p. 238°), identified by its acetyl derivative (m. p. 129°).

Anhydro-4-amino-1-hydroxymethylnaphthalene.—α-Naphthylamine (1400 g.), concentrated hydrochloric acid (1126 g.),

water (12 l.), and 37·5% aqueous formaldehyde solution (1176 c.c.) are stirred together for 20 hours below 20°. The mixture is made alkaline, and the anhydro-4-amino-compound, a reddish powder, is filtered off, washed, dried, mixed with calcium hydroxide (1600 g.), and dry distilled. Yield, 735 g. (oil). Fractions: < 300°, 34 g.; 300—305°, 116 g.; 305—310°, 199 g.; 310—315°, 106 g.; 315—320°, 14 g.; 320—340°, 45 g. These fractions consist mainly of α-naphthylamine (b. p. 300°) and 4-methyl-1-naphthylamine (b. p. 309—310°). They are separable by means of their picrates. The oil is dissolved in a minimum amount of boiling alcohol, and a slight excess of picric acid in boiling alcohol added. On cooling, the less soluble 4-methyl-1-naphthylamine picrate separates; it is recrystallised from alcohol to constant m. p., 205° (decomp.). The picrate is decomposed by hot sodium carbonate solution, and pure 4-methyl-1-naphthylamine is obtained (m. p. 49°).

Dry Distillation of Anhydro-4-methylaminobenzyl Alcohol.—This substance (45 g.) and calcium hydroxide (45 g.) on distillation afford 27 g. of oil. Fractions: 208—211°, 15 g.; 211—220°, 3 g. The fractions contain some *p*-toluidine (b. p. 200°) but mainly *N*-methyl-*p*-toluidine (b. p. 212°), identified by its nitroso-derivative (m. p. 49°).

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[*Received, November 24th*, 1943.]

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42. *The Action of Cuprous Oxide on Diazotised Amines. Part III. Action in Sulphuric Acid–Glacial Acetic Acid.*

By HERBERT H. HODGSON, STANLEY BIRTWELL, and EWART MARSDEN.

In the amines of the naphthalene series deamination by cuprous oxide in sulphuric acid–glacial acetic acid (where the amount of water is at a minimum) attains over 70% efficiency, but it falls below 40% in the benzene series. In all cases the positivity of the carbon atom to which the diazo-group is attached plays an important rôle in the deamination.

THE work reported in Parts I and II (Hodgson and H. Turner, J., 1942, 748; 1943, 86) had been carried out in various solvents which themselves participated in the reaction and to that extent facilitated it. Also, work by Hodgson, Leigh, and G. Turner, (J., 1942, 744) on the decomposition of aqueous diazonium salt solutions showed that the formation of symmetrical azo-compounds predominated over deamination. It appeared therefore of interest to examine in detail the action of cuprous oxide on diazonium salts in concentrated sulphuric–glacial acetic acid solution (*i.e.*, with the minimum of water present) as effected either by Hodgson and Walker's method (J., 1933, 1620) or by an inverted modification of it, especially as a yield of 82% of 1 : 3-dinitronaphthalene had been obtained thereby from 2 : 4-dinitro-1-naphthylamine. Further, in view of its success in the deamination of substituted naphthylamines, an extension of the method to amines of the benzene series appeared to be necessary.

The mechanism of deamination, when this takes place, would seem to be the intermediate formation of the highly reactive cuprous sulphate and subsequently of nascent copper, which would make the deamination a combined reduction assisted by copper as catalyst. In the naphthalene series excellent yields of deaminated products were obtained from diazotised nitronaphthylamines, but much inferior deamination was afforded by the various aniline derivatives examined. In all cases, however, the positivity of the carbon to which the diazo-group is attached is an important factor for the efficiency of the deamination, particularly in the naphthalene series, where an almost exact parallel between positivity and deamination is obtained, as shown in the sequences: *Naphthalene series*: 2 : 4-Dinitro-1-naphthylamine > 4-chloro- and 4-bromo-2-nitro-1-naphthylamine > 2-nitro-1-naphthylamine > 4-nitro-1-naphthylamine > 2-naphthylamine. *Benzene series*: 3-nitro-4-toluidine > 2 : 5-dichloroaniline > 2-nitroaniline > 2-nitro-4-toluidine > *p*-toluidine > benzidine > *p*-nitroaniline > aniline (which gave diphenyl and only a trace of benzene).

The low yield of nitrobenzene from *p*-nitroaniline, and the formation of diphenyl from aniline, indicate that there is the competing reaction of diaryl formation in the benzene series under the experimental conditions; nevertheless, the results in the benzene series are generally in the order of the positivity of the significant carbon.

EXPERIMENTAL.

General Procedure.—(a) *Direct.* The amine (0·1 g.-mol.), dissolved in glacial acetic acid (150 c.c.), was added below 20° to a solution of sodium nitrite (7·7 g.) in sulphuric acid (40 c.c., *d* 1·84), and, after 30 mins.' stirring, cuprous oxide (30—35 g.) was added during 20—30 mins. If the reaction was vigorous, the temperature was maintained at 20—30° by water cooling, but if it was relatively sluggish, the temperature was allowed to rise to 40—50°. Stirring was continued for about an hour after all the cuprous oxide had been added, the end-point being when the intense yellow or red diazo-solution had changed to light or straw-yellow. Isolation of the reaction product was effected either by pouring the mixture into water, followed by steam distillation, or by the addition of more glacial acetic acid followed by filtration, dilution with water, and steam distillation.

(b) *Indirect.* The amine (0·1 g.-mol.), dissolved in the minimum of sulphuric acid (*d* 1·84), was added below 20° to the above solution of nitrosylsulphuric acid, and the mixture stirred gradually into glacial acetic acid (150 c.c.), the subsequent procedure being as above. This method was employed for 2 : 4-dinitro-1-naphthylamine especially, but is applicable to the other amines.

(c) *With suspensions, e.g., deamination of 4-chloro- and 4-bromo-2-nitro-1-naphthylamine.* A mixture of the amine (11·1 g. of chloro-, or 13·35 g. of bromo-; 0·05 g.-mol.) suspended in glacial acetic acid (110 c.c.) was added to a solution of sodium nitrite (4·5 g.) in sulphuric acid (30 c.c., *d* 1·84) below 20°, and stirring continued for 30 mins. to complete the diazotisation. Finely powdered commercial cuprous oxide (17 g.) was then gradually stirred into the diazonium solution during 20 mins. with external water cooling, the subsequent procedure being as above.

When the deaminated product was only slightly or not volatile in steam, the by-product if steam volatile was so

removed, and the residue then crystallised from ethylene dichloride, acetone, or other suitable solvents. The results are summarised in the following table.

Amine (0·1 g.-mol.).	Deaminated product.	Yield, g.	Yield, %.
2 : 4-Dinitro-1-naphthylamine	1 : 3-Dinitronaphthalene	18·0	82·0
4-Chloro-2-nitro-1-naphthylamine	1-Chloro-3-nitronaphthalene	15·4	75·0
4-Bromo-2-nitro-1-naphthylamine	1-Bromo-3-nitronaphthalene	19·0	75·5
2-Nitro-1-naphthylamine	2-Nitronaphthalene	12·2	70·0
4-Nitro-1-naphthylamine	1-Nitronaphthalene	11·8	68·0
2-Naphthylamine	Naphthalene	6·0	47·0
3-Nitro-4-toluidine	3-Nitrotoluene	5·3	39·0
2 : 5-Dichloroaniline	1 : 4-Dichlorobenzene	5·0	35·0
2-Nitroaniline	Nitrobenzene	3·5	28·0
2-Nitro-4-toluidine	2-Nitrotoluene	3·56	26·0
p-Toluidine	Toluene	2·2	24·0
Benzidine	Diphenyl	3·5	23·0
p-Nitroaniline	Nitrobenzene	2·68	21·6
Aniline	Diphenyl (only a trace of benzene)	2·0	26·0

The authors thank I.C.I. Ltd., Dyestuffs Division, for gifts of chemicals.

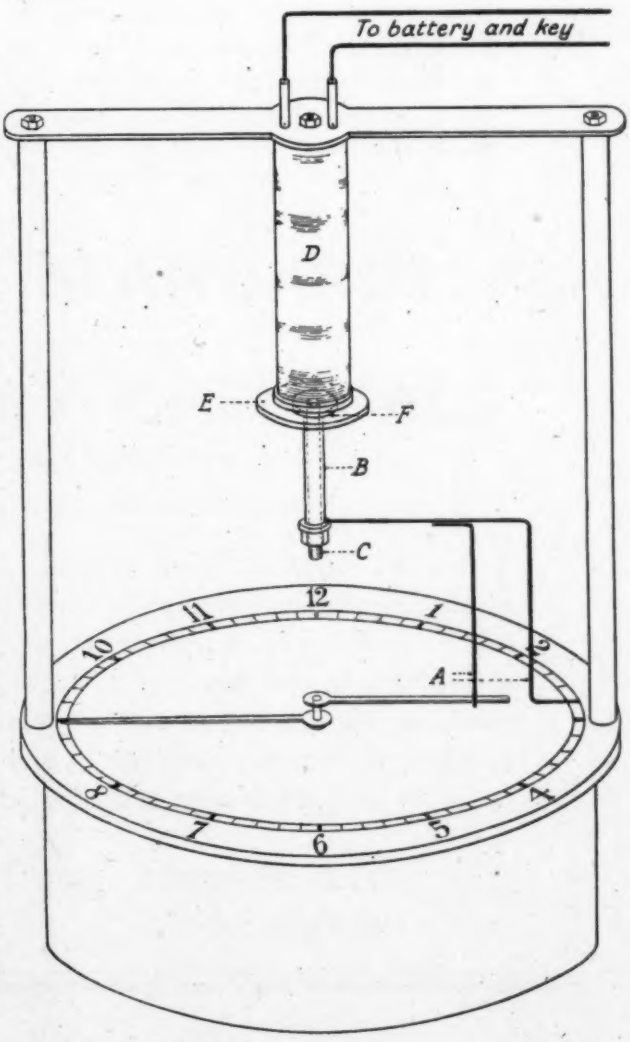
TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, December 1st*, 1943.]

NOTE.

A Laboratory Timing Clock. By GILBERT F. SMITH.

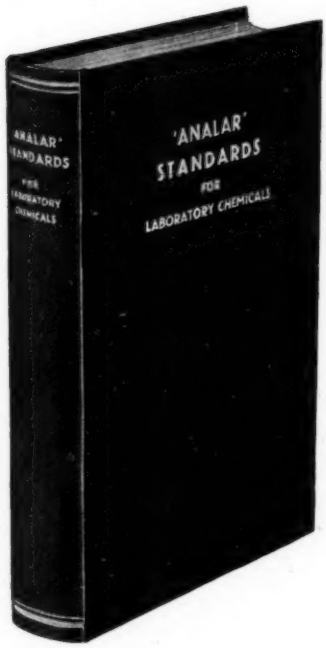
THE usual type of stop-clock records the time interval between two events with an accuracy of at least 1 sec., but is less accurate if a large number of successive events have to be timed while the clock is going. The clock now described does not suffer from this disadvantage and allows the timing of any number of successive events to about ¼ sec.

An electric clock of sufficient power to turn a 12" hand is required. The glass and the hour hand are removed, and the second hand is slightly shortened and provided with a rider *A* (see fig.) made of stiff steel wire. One prong of the rider serves as a pointer to indicate seconds on the scale, and the other engages on the forward edge of the seconds hand. The rider can rotate coaxially with the seconds hand and can also move upwards sufficiently far to disengage from the hand. To obtain these motions the rider is soldered to a brass tube *B*, which is a sliding fit over a thin steel rod *C*, and this is itself fixed firmly into a hole drilled into the centre of the lower face of a 6-volt electromagnet *D*, suspended as shown over the centre of the clock. A thin iron disc *E* is soldered round the top of tube *B*. By means of the hexagon nut at the bottom of the steel rod the rider assembly is adjusted so that the disc *E* is clear of the lower face *F* of the electromagnet.



When the clock is running, the seconds hand drives the rider round in front of it. In order to take a reading the electromagnet is energised by completing the electric circuit by means of a tapping key. This raises the rider clear of the hand and at the same time stops it, so that the reading given by the pointer can be made at leisure. The clock is ready for a second reading when the key is released and the rider is turned backwards by means of the iron disc to re-engage with the oncoming hand. At least four readings per minute can easily be made. The clock is used lying horizontally, and any tendency of the rider to overrun the hand is avoided by using a stiff lubricant, such as vaselin, in the rider bearing.

A clock of this type has been in use in these laboratories for several years, and despite its simple construction, it has never given trouble. It has been extremely useful in measuring the relatively small time intervals which are often required in experiments on chemical kinetics.—THE UNIVERSITY, LEEDS. [*Received, January 5th*, 1944.]



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